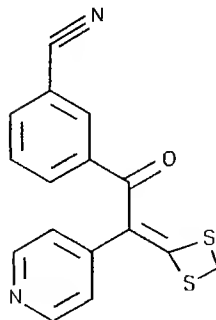
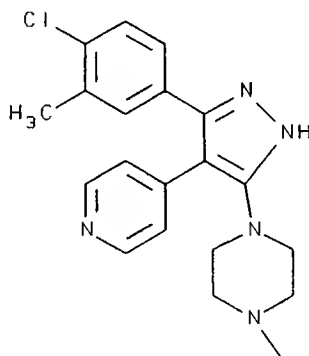


## Example A-406



5 mp 168.6-168.7 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>/300 MHz) 8.54 (dd, 2H, *J* = 4.6, 1.8 Hz), 7.68-7.62 (m 2H), 7.43-7.39 (m, 1H), 7.33-7.28 (m, 1H), 6.99 (dd, 2H, *J* = 4.4, 1.6 Hz), 4.22 (s, 2H); ESHRMS *m/z* 311.0330 (M+H, C<sub>16</sub>H<sub>10</sub>N<sub>2</sub>OS<sub>2</sub> requires 311.0313); Anal. Calc'd. for C<sub>16</sub>H<sub>10</sub>N<sub>2</sub>OS<sub>2</sub>: C, 61.91; H, 3.25; N, 9.02. Found: C, 61.45; H, 3.18; N, 8.91.

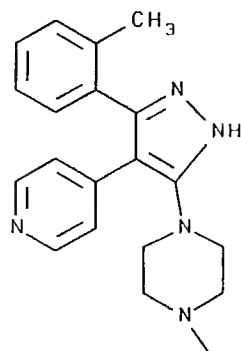
## Example A-407



15 1-[5-(3-methyl-4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-4-methylpiperazine.

mp 236.7-239.3 °C; <sup>1</sup>H NMR (DMSO-d<sub>6</sub>/300 MHz) 12.6 (brs, 1H), 8.45 (m, 2H), 7.41 (m, 1H), 7.26 (m, 3H), 7.0 (m, 1H), 2.86 (m, 4H), 2.35 (m, 4H), 2.27 (s, 3H), 2.16 (s, 3H); ESHRMS *m/z* 368.4653 (M+H, C<sub>20</sub>H<sub>22</sub>ClN<sub>5</sub> requires 368.1642).

## Example A-408

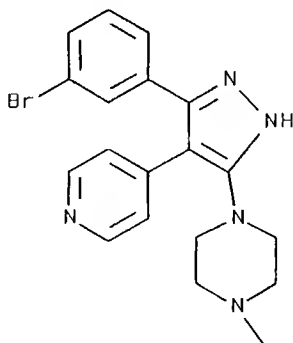


5            1-[5-(2-tolyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-4-methylpiperazine.

mp 244.0-244.2 °C; <sup>1</sup>H NMR (acetone-d<sub>6</sub>/300 MHz) 11.6 (brs, 1H), 8.35 (m, 2H), 7.35 (m, 2H), 7.25 (m, 4H), 3.05 (m, 4H), 2.47 (m, 4H), 2.25 (s, 3H), 2.00 (s, 3H);  
 10            ESHRMS *m/z* 334.2018 (M+H, C<sub>20</sub>H<sub>23</sub>N<sub>5</sub> requires 334.2032);  
 Anal. Calc'd for C<sub>20</sub>H<sub>23</sub>N<sub>5</sub>: C, 72.04; H, 6.95; N, 21.00.  
 Found: C, 72.03; H, 7.00; N, 20.85.

15

## Example A-409

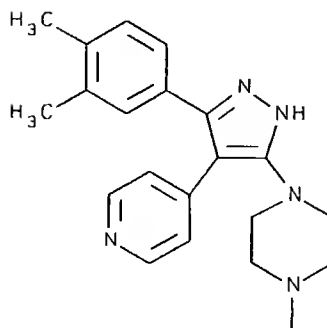


20            1-[5-(3-bromophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-4-methylpiperazine.

mp 222.5-223.4 °C; <sup>1</sup>H NMR (acetone-d<sub>6</sub>/300 MHz) 11.8 (brs, 1H), 8.51 (m, 2H), 7.55 (m, 2H), 7.34 (m, 4H), 3.0 (m, 4H), 2.41 (m, 4H), 2.22 (s, 3H); ESHRMS *m/z* 398.0982  
 25            (M+H, C<sub>19</sub>H<sub>20</sub>BrN<sub>5</sub> requires 398.0980).

403

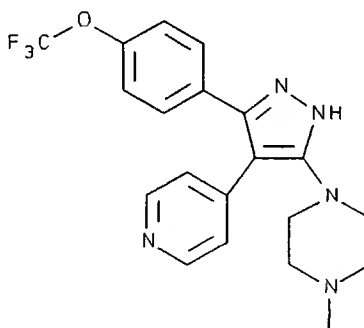
**Example A-410**



1- [5- (3,4-dimethylphenyl) -4- (4-pyridinyl) -1H-  
pyrazol-3-yl] -4-methylpiperazine.

mp 270.9-272.7 °C; <sup>1</sup>H NMR (DMSO-d<sub>6</sub>/300 MHz) 12.5  
(brs, 1H), 8.41 (m, 2H), 7.24 (m, 2H), 7.26 (m, 3H), 7.10  
(m, 2H), 6.92 (m, 1H), 2.86 (m, 4H), 2.38 (m, 4H), 2.21  
(s, 3H), 2.19 (s, 3H), 2.16 (s, 3H); ESHRMS m/z 348.2183  
(M+H, C<sub>21</sub>H<sub>25</sub>N<sub>5</sub> requires 348.2188).

**Example A-411**

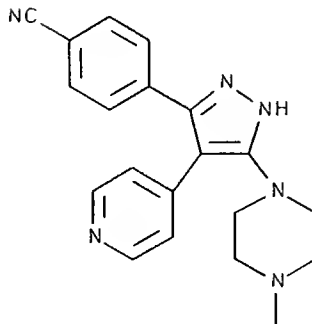


1- [5- (4-trifluoromethoxyphenyl) -4- (4-pyridinyl) -1H-  
pyrazol-3-yl] -4-methylpiperazine.

mp 221.0-221.2 °C; <sup>1</sup>H NMR (DMSO-d<sub>6</sub>/300 MHz) 12.7  
(brs, 1H), 8.45 (m, 2H), 7.38 (s, 4H), 7.24 (m, 2H), 2.86  
(m, 4H), 2.34 (m, 4H), 2.16 (s, 3H); ESHRMS m/z 404.1698  
(M+H, C<sub>20</sub>H<sub>20</sub>F<sub>3</sub>N<sub>5</sub>O requires 404.1698).

404

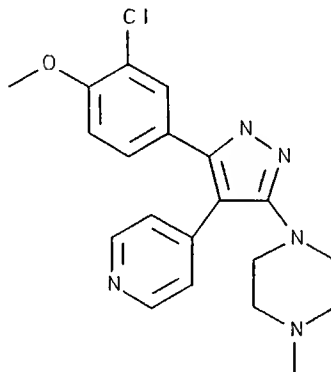
**Example A-412**



5            1-[5-(4-cyanophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-4-methylpiperazine.

mp > 300 °C; <sup>1</sup>H NMR (DMSO-d<sub>6</sub>/300 MHz) 12.8 (brs, 1H), 8.47 (m, 2H), 7.83 (m, 2H), 7.42 (m, 2H), 2.88 (m, 4H), 2.39 (m, 4H), 2.20 (s, 3H); ESHRMS *m/z* 345.1848  
10 (M+H, C<sub>20</sub>H<sub>20</sub>N<sub>6</sub> requires 345.1828).

**Example A-413**



15

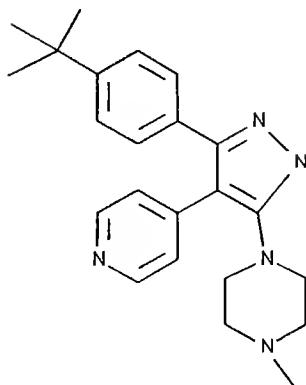
1-[5-(3-chloro-4-methoxyphenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-4-methylpiperazine.

20            mp 272.7-276.4 °C; <sup>1</sup>H NMR (DMSO-d<sub>6</sub>/300 MHz) 8.44 (dd, 2H, *J* = 4.6, 1.6 Hz), 7.32-7.13 (m, 5H), 3.84 (s, 3H), 2.90-2.85 (m, 4H), 2.38-2.35 (m, 4H), 2.16 (s, 3H); ESHRMS *m/z* 384.1580 (M+H C<sub>20</sub>H<sub>22</sub>ClN<sub>5</sub>O requires 384.1591).

25

405

## Example A-414



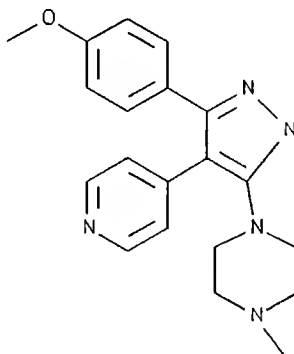
5

1-[5-(4-tert-butylphenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-4-methylpiperazine.

mp 243.6-244.3 °C; <sup>1</sup>H NMR (DMSO-d<sub>6</sub>/300 MHz) 8.44 (dd, 2H, *J* = 4.6, 1.6, Hz), 7.40 (d, 2H, *J* = 8.3 Hz), 7.28-7.18 (m, 4H), 2.90-2.85 (m, 4H), 2.38-2.34 (m, 4H), 2.16 (s, 3H), 1.26 (s, 9H); ESHRMS *m/z* 376.2491 (M+H, C<sub>23</sub>H<sub>29</sub>N<sub>5</sub> requires 376.2501).

15

## Example A-415



1-[4-(4-methoxyphenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-4-methylpiperazine.

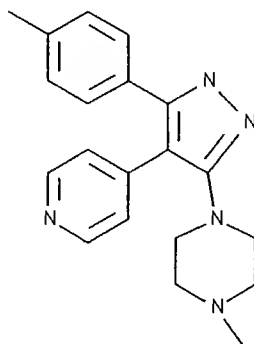
20

mp 259.0-260.2 °C; <sup>1</sup>H NMR (DMSO-d<sub>6</sub>/300 MHz) 8.53 (dd, 2H, *J* = 4.4, 1.6 Hz), 7.24 (dd, 2H, *J* = 4.4, 1.6 Hz), 7.18 (d, 2H, *J* = 8.9 Hz), 6.94 (d, 2H, *J* = 8.9 Hz),

406

3.75 (s, 3H), 2.90-2.85 (m, 4H), 2.39-2.35 (m, 4H), 2.16 (s, 3H); ESHRMS  $m/z$  350.1991 (M+H,  $C_{20}H_{23}N_5O$  requires 350.1981); Anal. Calc'd. for  $C_{20}H_{23}N_5O + 3.93\%H_2O$ : C, 66.04; H, 6.81; N, 19.25. Found: C, 66.01; H, 6.62; N, 19.32.

**Example A-416**



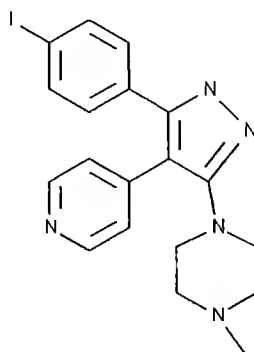
10

1-[5-(4-methylphenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-4-methylpiperazine.

mp 243.0-246.8 °C;  $^1H$  NMR (DMSO- $d_6$ /300 MHz) 8.41 (dd, 2H,  $J = 4.6, 1.6$  Hz), 7.24 (m, 6H), 2.91-2.86 (m, 4H), 2.40-2.35 (m, 4H), 2.29 (s, 3H), 2.16 (s, 3H); ESHRMS  $m/z$  334.2041 (M+H,  $C_{20}H_{23}N_5$  requires 334.2032); Anal. Calc'd for  $C_{20}H_{23}N_5 + 4.09\%H_2O$ : C, 69.10; H, 7.13; N, 20.14. Found: C, 69.10; H, 7.08; N, 20.13.

20

**Example A-417**



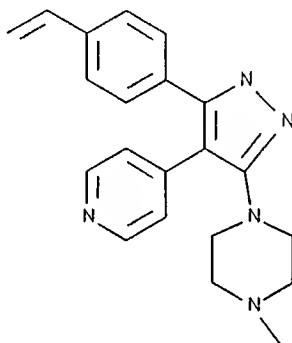
25

407

1-[5-(4-iodophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-4-methylpiperazine.

mp 265.2-265.8 °C; <sup>1</sup>H NMR (CD<sub>3</sub>OD/300 MHz) 8.41 (dd, 2H, *J* = 4.6, 1.6 Hz), 7.76-7.74 (m, 2H), 7.41-7.39 (m, 2H), 7.08-7.05 (m, 2H), 3.08-3.04 (m, 4H), 2.61-2.58 (m, 4H), 2.35 (s, 3H); ESHRMS *m/z* 446.0847 (M+H, C<sub>19</sub>H<sub>20</sub>IN<sub>5</sub> requires 446.0842); Anal. Calc'd. for C<sub>19</sub>H<sub>20</sub>IN<sub>5</sub> + 12.09%H<sub>2</sub>O: C, 44.60; H, 5.39; N, 13.69. Found: C, 44.50; H, 4.56; N, 13.66.

**Example A-418**

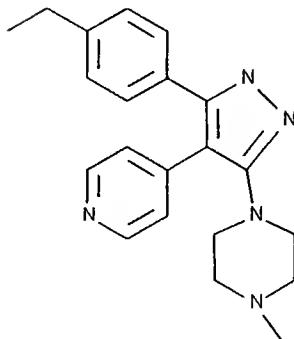


1-[5-(4-ethenylphenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-4-methylpiperazine.

mp >300 °C; <sup>1</sup>H NMR (CD<sub>3</sub>OD/300 MHz) 8.49 (dd, 2H, *J* = 4.6, 1.6 Hz), 7.47-7.44 (m, 4H), 7.26 (d, 2H, *J* = 8.4 Hz), 6.75 (dd, *J* = 17.7, 11.1 Hz), 5.83 (d, 1H, *J* = 17.5 Hz), 5.28 (d, 1H, *J* = 11.1 Hz), 3.07-3.03 (m, 4H), 2.58-2.53 (m, 4H), 2.31 (s, 3H); ESHRMS *m/z* 346.2034 (M+H, C<sub>21</sub>H<sub>23</sub>N<sub>5</sub> requires 346.2032); Anal. Calc'd. for C<sub>21</sub>H<sub>23</sub>N<sub>5</sub> + 2.83%H<sub>2</sub>O: C, 70.95; H, 6.84; N, 19.70. Found: C, 70.97; H, 6.49; N, 19.54.

408

Example A-419

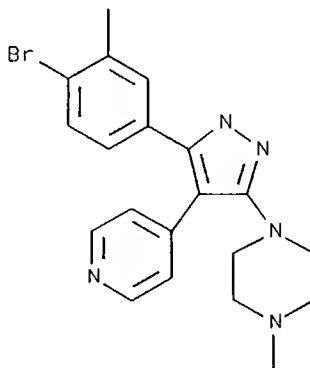


5            1-[5-(4-ethylphenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-4-methylpiperazine.

mp 221.6-222.6 °C; <sup>1</sup>H NMR (CD<sub>3</sub>OD/300 MHz) 8.38 (dd, 2H, *J* = 4.6, 1.6 Hz), 7.44-7.40 (m, 2H), 7.26-7.19 (m, 4H), 3.06-3.02 (m, 4H), 2.66 (q, 2H, *J* = 7.5 Hz), 2.59-2.54 (m, 4H), 2.32 (s, 3H), 1.23 (t, 3H, *J* = 7.5 Hz);  
 10            ESHRMS *m/z* 348.2188 (M+H, C<sub>21</sub>H<sub>25</sub>N<sub>5</sub> requires 348.2188);  
 Anal. Calc'd for C<sub>21</sub>H<sub>25</sub>N<sub>5</sub> + 2.59% H<sub>2</sub>O: C, 70.71; H, 7.35; N, 19.63. Found: C, 70.76; H, 7.40; N, 19.46.

15

Example A-420



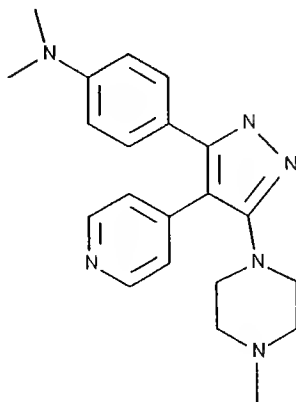
20            1-[5-(4-bromo-3-methylphenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-4-methylpiperazine.

mp 294.7 °C decomp.; <sup>1</sup>H NMR (CD<sub>3</sub>OD/300 MHz) 8.41 (dd, 2H, *J* = 4.6, 1.6 Hz), 7.55 (d, 1H, *J* = 8.2 Hz),  
 25            7.45-7.42 (m, 2H), 7.27-7.25 (m, 1H), 7.00-6.97 (m 2H),

409

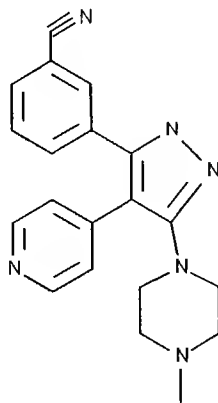
3.08-3.03 (m, 4H), 2.59-2.54 (m, 4H), 2.35 (s, 3H), 2.31 (s, 3H); ESHRMS  $m/z$  412.1124 (M+H,  $C_{20}H_{22}BrN_5$  requires 412.1137).

5

**Example A-421**

10 1-[5-(4-dimethylaminophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-4-methylpiperazine.

mp >300 °C (decomposed);  $^1H$  NMR ( $CD_3OD$  / 300 MHz) 8.37 (d, 2H,  $J$  = 4.6 Hz), 7.44 (d, 2H,  $J$  = 4.8 Hz), 7.12, (d, 2H,  $J$  = 8.9 Hz), 6.73 (d, 2H,  $J$  = 8.7 Hz), 3.04-3.02  
15 (m, 4H), 2.96 (s, 6H), 2.54-2.49 (m, 4H), 2.31 (s, 3H); ESHRMS  $m/z$  363.2266 (M+H,  $C_{21}H_{26}N_6$  requires 363.22972).

**Example A-422**

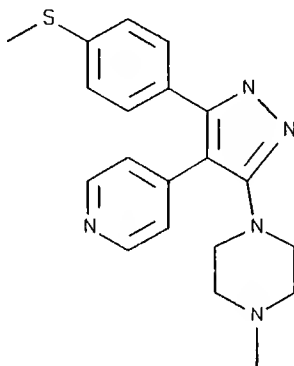
20

1-[5-(3-cyanophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-4-methylpiperazine.

410

mp 223.4-224.3 °C; <sup>1</sup>H NMR (CD<sub>3</sub>OD / 300 MHz) 8.44 (dd, 2H, J= 4.6, 1.4 Hz), 7.75-7.69 (m, 2H), 7.56-7.54 (m, 2H), 7.40-7.38 (m, 2H), 3.05-3.03 (m, 4H), 2.54-2.49 (m, 4H), 2.53 (s, 3H); ESHRMS m/z 345.1840 (M+H, C<sub>20</sub>H<sub>20</sub>N<sub>6</sub> requires 345.1828).

**Example A-423**



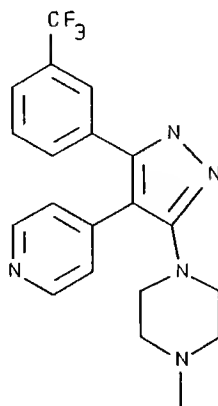
10

1-[5-(4-thiomethoxyphenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-4-methylpiperazine.

mp 275.6-281.9 °C; <sup>1</sup>H NMR (CD<sub>3</sub>OD / 300 MHz) 8.44-8.40 (m, 2H), 7.46-7.41 (m, 2H), 7.28-7.23 (m, 4H), 3.04-3.00 (m, 4H), 2.59-2.53 (M, 4H), 2.48 (s, 3H), 2.31 (s, 3H); ESHRMS m/z 366.1777 (M+H, C<sub>20</sub>H<sub>23</sub>N<sub>5</sub>S requires 366.1752).

20

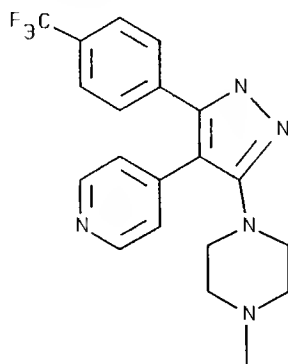
**Example A-424**



411

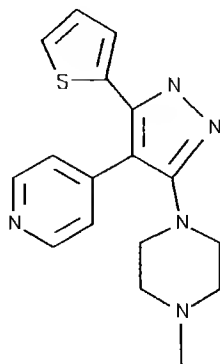
1- [5- (3-trifluoromethylphenyl) -4- (4-pyridinyl-1H-pyrazol-3-yl) -4-methylpiperazine.

mp 212.6-213.7 °C; <sup>1</sup>H NMR (CD<sub>3</sub>OD / 300 MHz) 8.43 (d, 2H, *J* = 4.8 Hz), 7.69-7.56 (m, 4H), 7.41 (s, 2H), 3.07-3.04 (m, 4H), 2.56-2.53 (m, 4H), 2.32 (s, 3H); ESHRMS *m/z* 388.1764 (M+H, C<sub>20</sub>H<sub>20</sub>F<sub>3</sub>N<sub>5</sub> requires 388.1749).

**Example A-425**

1- [5- (4-trifluoromethylphenyl) -4- (4-pyridinyl-1H-pyrazol-3-yl) -4-methylpiperazine.

mp 240.5 °C (decomposed); <sup>1</sup>H NMR (CD<sub>3</sub>OD / 300 MHz) 8.43 (dd, 2H, *J* = 4.6, 1.6 Hz), 7.70-7.67 (m, 2H), 7.51-7.48 (m, 2H), 7.42-7.38 (m 2H), 3.09-3.04 (m, 4H), 2.59-2.53 (m, 4H), 2.31 (s, 3H); ESHRMS *m/z* 388.1768 (M+H, C<sub>20</sub>H<sub>20</sub>F<sub>3</sub>N<sub>5</sub> requires 388.1749).

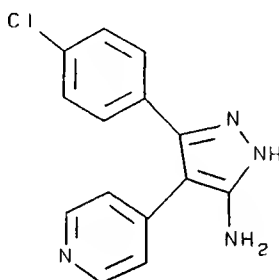
**Example A-426**

1-[5-(2-thienyl)-4-(4-pyridinyl-1H-pyrazol-3-yl)]-4-methylpiperazine.

mp 199.7 °C (decomposed); <sup>1</sup>H NMR (CD<sub>3</sub>OD / 300 MHz)  
 5 8.44 (d, 2H, *J* = 5.8 Hz), 7.47 (d, 2H, *J* = 5.6 Hz), 7.13  
 - 7.07 (m, 3H), 3.04-3.00 (m, 4H), 2.53-2.49 (m, 4H),  
 2.30 (s, 3H); ESHRMS *m/z* 326.1454 (M+H, C<sub>17</sub>H<sub>19</sub>N<sub>5</sub>S  
 requires 326.1439).

10

### Example A-427



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#### Step 1: Preparation of 3-dimethylamino-1-(4-chlorophenyl)-2-(pyridin-4-yl)-2-propene-1-one

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A solution of 4-chlorophenyl-2-(pyridin-4-yl)ethan-1-one (20.0 g, 86.4 mmol) and N,N-dimethylformamide dimethylacetal (57.6 mL, 0.43 mole) was heated at 100 °C  
 for 3 ½ hours. The reaction mixture was concentrated in  
 vacuo, and the residue crystallized from methyl butyl  
 ether to give 3-dimethylamino-1-(4-chlorophenyl)-2-  
 (pyridin-4-yl)-2-propen-1-one (22.80 g, 93%). <sup>1</sup>H NMR  
 (CDCl<sub>3</sub>/300 MHz) δ 8.52 (d, 2H), 7.38 (d, 2H), 7.29 (d,  
 2H), 7.08 (d, 2H), 2.83 (s, 6H).

#### Step 2: Preparation of 5-(4-chlorophenyl)-4-(pyridin-4-yl)isoxazole

30

A solution of 3-dimethylamino-1-(4-chlorophenyl)-2-  
 (pyridin-4-yl)-2-propen-1-one (22.80 g, 79.7 mmol),  
 hydroxylamine hydrochloride (18.01 g, 0.26 mole), and 150

mL ethanol was heated to reflux for 30 minutes. The reaction mixture was then cooled to room temperature and concentrated *in vacuo*. The residue was dissolved in 1N hydrochloric acid and then treated with an aqueous saturated solution of sodium bicarbonate. The precipitates were collected by filtration, washed with water and ethanol, and dried to yield 5-(4-chlorophenyl)-4-(pyridin-4-yl)isoxazole (20.50 g, 93%). m.p. 120.8-120.9 °C. <sup>1</sup>H NMR (CDCl<sub>3</sub>/CD<sub>3</sub>OD/300 MHz) δ 8.53 (d, 2H), 8.46 (s, 1H), 7.51 (d, 2H), 7.41-7.34 (m, 4H). ESLRMS *m/z* 257 (M+H). ESHRMS *m/z* 257.0457 (M+H, C<sub>14</sub>H<sub>9</sub>N<sub>2</sub>OCl requires 257.0482).

Step 3: Preparation of 3-(4-chlorophenyl)-3-oxo-2-(pyridin-4-yl)propanenitrile:

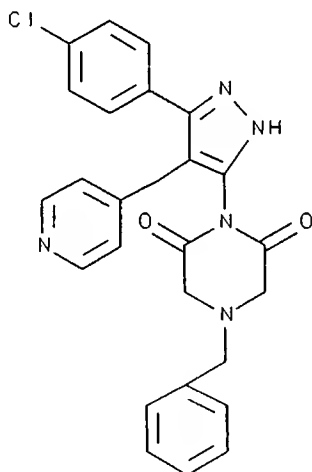
A solution of 5-(4-chlorophenyl)-4-(pyridin-4-yl)isoxazole (20.5 g, 79.9 mmol) and 150 mL of a 1N sodium hydroxide solution was stirred at 60 °C for 1 hour. The reaction mixture was cooled to room temperature and adjusted to pH 6 with concentrated hydrochloric acid. The precipitates were filtered, washed with water and ethanol, and dried to give 3-(4-chlorophenyl)-3-oxo-2-(pyridin-4-yl)propanenitrile (20.0 g, quantitative yield). m.p. 225.4-234.9 °C. <sup>1</sup>H NMR (CDCl<sub>3</sub>/CD<sub>3</sub>OD/300 MHz) δ 8.12 (brs, 2H), 7.73-7.59 (m, 5H), 7.30 (d, 3H). ESLRMS *m/z* 257 (M+H). ESHRMS *m/z* 257.0481 (M+H, C<sub>14</sub>H<sub>9</sub>N<sub>2</sub>OCl requires 257.0482).

Step 4: 5-amino-3-(4-chlorophenyl)-4-(pyridin-4-yl)-pyrazole

A solution of 3-(4-chlorophenyl)-3-oxo-2-(pyridin-4-yl)propanenitrile (3.50 g, 13.6 mmol) in 40 mL acetonitrile and phosphorous trichloride (14.2 mL, 163 mmol) was stirred at 100 °C for 5 hours. The reaction

mixture was concentrated in vacuo, and the residue taken up in toluene and concentrated again. The residue was then taken up in ethanol (150 mL) and treated with anhydrous hydrazine (1.71 mL, 54.4 mmol). The reaction mixture was heated to reflux for 3 hours, cooled, and concentrated in vacuo. The residue was triturated with a mixture of ethanol and dichloromethane (1:4), and filtered. The solid was washed with the ethanol/dichloromethane mixture, and dried to give 5-amino-3-(4-chlorophenyl)-4-(pyridin-4-yl)-pyrazole (2.0 g, 54%): m.p. >300 °C. <sup>1</sup>H NMR (DMSO/300 MHz) δ 8.40 (d, 2H), 7.40 (d, 2H), 7.29 (d, 2H), 7.11 (d, 2H), 5.05 (s, 2H). ESLRMS *m/z* 271 (M+H). ESHRMS *m/z* 271.0752 (M+H, C<sub>14</sub>H<sub>11</sub>N<sub>4</sub>Cl requires 271.0750).

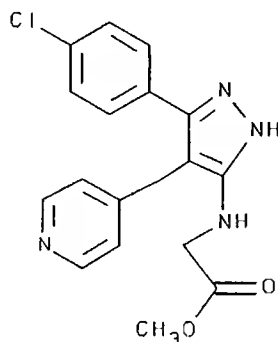
#### Example A-428



A solution of 1,1'-carbonyldiimidazole (1.19 g, 7.38 mmol) and N-benzyliminodiacetic acid (0.824 g, 3.69 mmol) in dimethylformamide was heated at 75 °C for 30 minutes. To this mixture the 5-amino-3-(4-chlorophenyl)-4-(pyridin-4-yl)-pyrazole (1.0 g, 3.69 mmol) was added, and heating was continued at 75 °C overnight. The white solid was filtered, was washed with diethyl ether, methylene chloride, 5% methanol/methylene chloride, and ethanol, and was dried to give the desired imide as an

off-white solid (0.9 g, 53%): m.p. >300 °C. <sup>1</sup>H NMR (DMSO/300 MHz) δ 8.53 (m, 2H), 7.5 (d, 2H), 7.44- 7.16 (m, 7H), 6.98 (m, 2H), 3.64 (m, 4H), 3.48 (m, 2H). ESLRMS m/z 458 (M+H). ESHRMS m/z 458.1380 (M+H, C<sub>25</sub>H<sub>20</sub>N<sub>5</sub>O<sub>2</sub>Cl requires 458.1384).

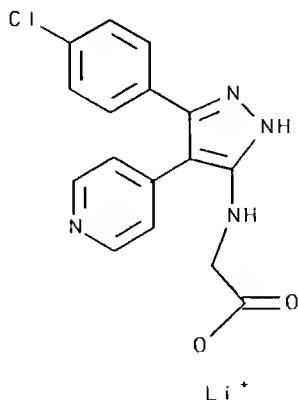
#### Example A-429



Methyl 2-{[3-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-5-yl]amino}acetate

A solution of 5-amino-3-(4-chlorophenyl)-4-(pyridin-4-yl)-pyrazole (1.0 g, 3.7 mmol) in dimethylformamide (30 mL) was heated to 95 °C and methyl bromo acetate (0.34 mL, 3.7 mmol) was added dropwise. The resulting solution was stirred at 95 °C for 4 hours, cooled, and concentrated in vacuo to an orange viscous oil (1.79 g). A portion of this product mixture (1.20 g) was crystallized from ethanol and diethyl ether to give methyl 2-{[3-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-5-yl]amino}acetate as a bright yellow solid (805 mg): m.p. 195.4-196.8 °C. <sup>1</sup>H NMR (CD<sub>3</sub>OD/300 MHz) δ 8.49 (d, 2H), 7.68 (d, 2H), 7.44 (m, 4H), 5.37 (s, 2H), 3.84 (s, 3H). ESLRMS m/z 343 (M+H). ESHRMS m/z 343.0975 (M+H, C<sub>17</sub>H<sub>16</sub>N<sub>4</sub>O<sub>2</sub>Cl requires 343.0962).

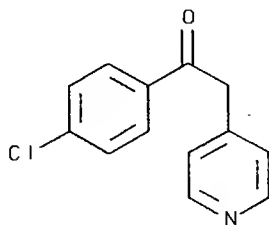
## Example A-430



5           Lithium 2-([3-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-5-yl]amino)acetate

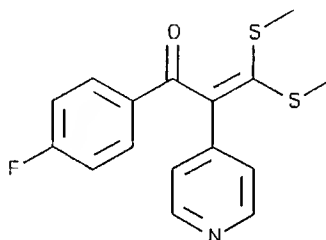
To a solution of methyl 2-([3-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-5-yl]amino)acetate (500 mg, 1.5  
 10 mmol) in 15 mL of methanol and 5 mL of water was added lithium hydroxide (189 mg, 4.5 mmol). The reaction mixture was stirred at room temperature for 5 hours. The solvent was removed *in vacuo*, and the residue taken up in ethanol. The precipitate was filtered and washed with  
 15 methanol, and the filtrate was concentrated to give lithium 2-([3-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-5-yl]amino)acetate as a yellow/orange solid (479 mg, 95%). mp >300 °C. <sup>1</sup>H NMR (CD<sub>3</sub>OD/300 MHz) δ 8.06 (d, 2H), 7.43 (d, 2H), 7.37 (m, 4H), 3.34 (s, 2H). ESLRMS m/z 329 (M+H), 335 (M+Li), 351 (M+Na). ESHRMS m/z 329.0772 (M+H, 20 C<sub>16</sub>H<sub>14</sub>N<sub>4</sub>O<sub>2</sub>Cl requires 329.0805).

## Example A-431

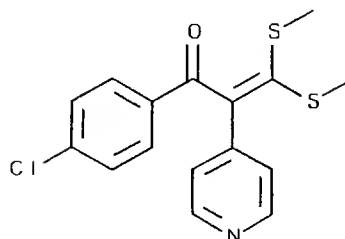


The above 4-chlorophenylketone was prepared according to the procedure used in Step 1 of Example C-1, infra, substituting methyl 4-chlorobenzoate for ethyl 4-fluorobenzoate. Yield; (74 %), yellow solid, mp = 95.5-97.3 °C; <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>/300 MHz) 8.57 (br d, 2H), 7.92 (d, 2H), 7.46 (d, 2H), 7.20 (d, 2H), 4.28 (s, 2H); ESLRMS m/z 232 (M+H).

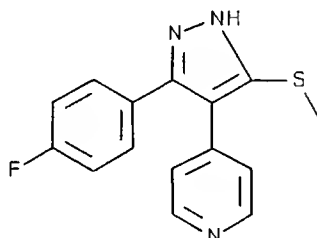
#### Example A-432



To the ketone (1.0gm, 4.7 mmol) from Step 1 of Example C-1, infra, in anhydrous tetrahydrofuran (10 mL) was added 1M potassium t-butoxide in tetrahydrofuran (10 mL, 10 mmol). The reaction mixture was stirred for 15 minutes at room temperature, then carbon disulfide (0.31 mL, 5.1 mmol) was added. After several minutes, methyl iodide (0.64 mL, 10.3 mmol) was added and the reaction allowed to stir for 4 hours. The reaction mixture was diluted with saturated sodium bicarbonate solution (25 mL) and extracted twice with ethyl acetate (35 mL). The combined ethyl acetate layers were washed with water (25 mL) and brine (25mL). The organic solution was dried (MgSO<sub>4</sub>), filtered and concentrated to an orange oil. The oil solidified on standing. Yield 1.4 gm (94%), mp 80.2-82.1 °C; <sup>1</sup>H-NMR (CDCl<sub>3</sub>/300 MHz) 8.59 (d, 2H), 7.96 (m, 2H), 7.38 (m, 2H), 7.14 (m, 2H), 2.33 (s, 3H), 2.23 (s, 3H); Anal. Calc'd for C<sub>16</sub>H<sub>14</sub>FNOS<sub>2</sub>: C, 60.16; H, 4.42; N, 4.39; S, 20.08. Found: C, 59.89; H, 4.09; N, 4.31; S, 20.14.

**Example A-433**

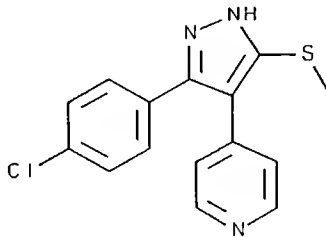
5       The above compound was prepared in a manner  
analogous to Example A-432 starting with the product of  
Example A-431. Crude yield: 100 %; mp 87.6-88.2 °C; <sup>1</sup>H-  
NMR (CDCl<sub>3</sub>/300 MHz) 8.60 (d, 2H), 7.87 (d, 2H), 7.44 (d,  
2H), 7.37 (m, 2H), 2.33 (s, 3H), 2.22 (s, 3H); ESHRMS *m/z*  
10 336.0297 (M+H, C<sub>16</sub>H<sub>15</sub>ClNOS<sub>2</sub> requires 336.0283); Anal.  
Calc'd for C<sub>16</sub>H<sub>14</sub>ClNOS<sub>2</sub>: C, 57.22; H, 4.20; N, 4.17.  
Found: C, 57.44; H, 3.97; N, 4.04.

**Example A-434**

15       To the compound of Example A-432 (1.4 gm, 4.4 mmol)  
in ethanol (15 mL) was added 1M hydrazine in acetic acid  
20 (5 mL, 5 mmol). The reaction was stirred at room  
temperature for 18 hours. No reaction had occurred, so  
additional hydrazine hydrate (1.08 mL, 22 mmol) was added  
and the reaction heated to reflux for 6 hours. The  
product began to precipitate from the reaction mixture.  
25 The reaction was cooled to room temperature and water was  
added to precipitate the product. The solid was  
collected by suction filtration and air dried. Yield:  
675 mg (53%). The product was recrystallized from  
ethanol: 494 mg; mp 249.9-249.9 °C; <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>/300

419

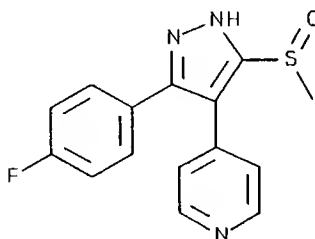
MHz) 13.51 (br s, 1H), 8.50 (d, 2H), 7.34 (m, 2H), 7.23 (m, 2H), 7.16 (m, 2H), 2.43 (s, 3H); ESHRMS  $m/z$  286.0807 (M+H,  $C_{15}H_{13}FN_3S$  requires 286.0814); Anal. Calc'd for  $C_{15}H_{12}FN_3S$ : C, 63.14; H, 4.24; N, 14.73. Found: C, 63.01; H, 4.43; N, 14.81.

**Example A-435**

10

The above compound was made in an analogous manner to Example A-434 starting with the compound of Example A-433. Yield: 750 mg (33%); mp 250.2-250.2 °C;  $^1H$  NMR (DMSO- $d_6$ /300 MHz) 13.57 (br s, 1H), 8.51 (m, 2H), 7.45 (br s, 2H), 7.32 (m, 2H), 7.17 (m, 2H), 2.43 (s, 3H); ESHRMS  $m/z$  302.0537 (M+H,  $C_{15}H_{13}ClN_3S$  requires 302.0518); Anal. Calc'd for  $C_{15}H_{12}ClN_3S$ : C, 59.70; H, 4.01; N, 13.92. Found: C, 59.56; H, 3.96; N, 13.96.

20

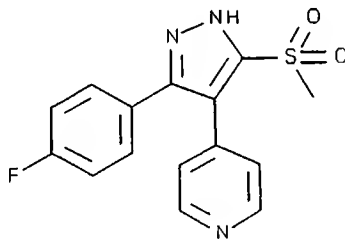
**Example A-436**

3-(4-fluorophenyl)-4-(methylsulfinyl)-4-pyridin-4-yl-1H-pyrazole

25

To the compound of Example A-434 (150 mg, 0.52 mmol) in ethanol (15 mL) was added ammonium persulfate (450 mg, 1.97 mmol). The reaction mixture was stirred at ambient

temperature. After several hours an additional amount of ammonium persulfate (450 mg) was added. The reaction mixture was monitored by TLC (silica) using 5% methanol in dichloromethane as the eluting solvent. When the  
5 stating material had been consumed, the reaction mixture was quenched with saturated sodium bicarbonate (25 mL) and extracted with ethyl acetate (2 x 25 mL). The ethyl acetate layers were combined, washed with brine (25 mL) and dried (MgSO<sub>4</sub>). Filtration and concentration produced  
10 a white solid. The solid was triturated with diethyl ether, collected by suction filtration, and air dried. Yield 150 mg (96%), mp 262.9-262.9 °C; <sup>1</sup>H NMR (DMSO-d<sub>6</sub>/300 MHz) 14.22 (br s, 1H), 8.56 (d, 2H), 7.42-7.23 (br m, 6H), 2.94 (s, 3H); Anal. Calc'd for C<sub>15</sub>H<sub>12</sub>FN<sub>3</sub>OS·0.25  
15 H<sub>2</sub>O: C, 58.91; H, 4.12; N, 13.74; Found: C, 58.88; H, 4.17; N, 13.39.

**Example A-437**

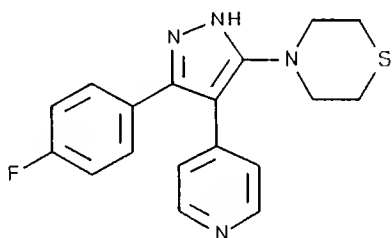
20

3-(4-fluorophenyl)-5-(methylsulfonyl)-4-pyridin-4-yl-1H-pyrazole

25 To the compound of Example A-434 (285 mg, 1 mmol) in ethanol (10 mL) was added potassium peroxymonosulfate (2.45 gm, 4 mmol) and water (5 mL). The reaction mixture was stirred at ambient temperature. After 6 hours the reaction mixture was diluted with water (20 mL) and  
30 extracted with ethyl acetate (2 x 30 mL). The ethyl acetate layers were combined, washed with brine (25 mL) and dried (MgSO<sub>4</sub>). The ethyl acetate did not efficiently extract the product from the aqueous phase, so the

aqueous layer was saturated with sodium chloride and extracted with acetonitrile (50 mL). The acetonitrile solution was dried ( $\text{MgSO}_4$ ), filtered, and combined with the filtered ethyl acetate solution. The solvents were  
5 evaporated and the resulting solid was triturated with a small amount of acetonitrile, collected by suction filtration, and air dried. Yield: 203 mg (64 %); mp  $297.1 \rightarrow 300^\circ\text{C}$ ;  $^1\text{H}$  NMR ( $\text{DMSO}-d_6/300\text{ MHz}$ ) 14.37 (br s, 1H), 8.54 (m, 2H), 7.29 (m, 6H), 3.26 (s, 3H); Anal.  
10 Calc'd for  $\text{C}_{15}\text{H}_{12}\text{FN}_3\text{O}_2\text{S}$ : C, 56.77; H, 3.81; N, 13.24. Found: C, 56.52; H, 4.03; N, 13.11.

#### Example A-438

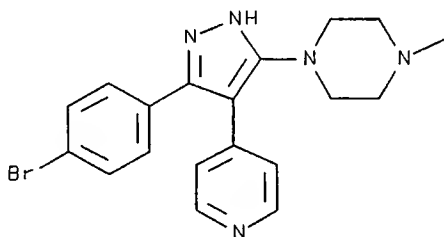


15

To the compound of Example A-432 (638 mg, 2 mmol) in toluene (6 mL) was added thiomorpholine (502  $\mu\text{L}$ , 5 mmol). The reaction mixture was heated to between  $80$  and  $110^\circ\text{C}$ .  
20 After about three hours the bis-thiomorpholine substituted product began to precipitate from the reaction mixture. When the dithioketene acetal had been completely consumed, the reaction mixture was cooled to room temperature and the insoluble bis-thiomorpholine  
25 compound removed by filtration. To the toluene solution was added hydrazine hydrate (1 mL) and sufficient ethanol to create a homogeneous solution. The reaction mixture was then stirred at room temperature for 72 hours. The reaction mixture was diluted with ethyl acetate (50 mL)  
30 and extracted twice with water (25 mL) and once with brine (25 mL). The organic solution was dried ( $\text{MgSO}_4$ ), filtered and concentrated to a reddish solid. The solid was triturated with acetonitrile, collected by suction

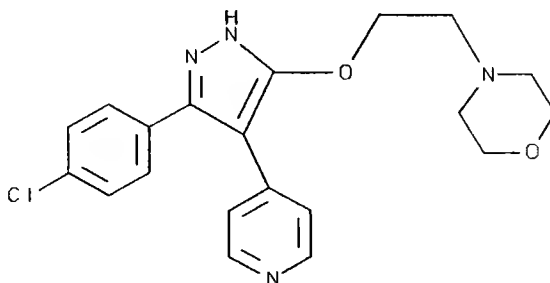
filtration, and dried in-vacuo. The solid was then suspended in acetonitrile and heated to reflux. Ethyl acetate was then added until the solid almost completely dissolved. A small amount of ethanol was then added and the homogeneous yellow solution concentrated until a solid began to form. Allow to cool to room temperature. Collected a white solid by suction filtration. Yield: 63 mg, (7%); <sup>1</sup>H NMR (DMSO-d<sub>6</sub>/300 MHz) 12.65 (br s, 1H), 8.45 (d, 2H), 7.27 (m, 6H), 3.14 (m, 4H), 2.63 (m, 4H). ESLRMS m/z 341 (M+H); ESHRMS m/z 341.1241 (M+H, C<sub>18</sub>H<sub>18</sub>FN<sub>4</sub>S requires 341.1236).

### Example A-439



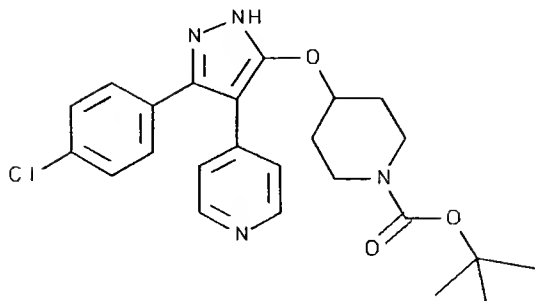
The above compound was prepared in a similar manner to Example A-438 starting with the appropriate dithioketene acetal and N-methylpiperazine. A white solid was obtained, mp 270.2-270.7 °C; <sup>1</sup>H NMR (DMSO-d6/300 MHz) 12.7 (br s, 1H), 8.47 (m, 2H), 7.57 (m, 2H), 7.21 (m, 2H), 2.85 (m, 4H), 2.34 (m, 4H) 2.15 (s, 3H); ESHRMS 398.0993 (M+H, C<sub>19</sub>H<sub>21</sub>BrN<sub>5</sub> requires 398.0980).

### Example A-440



To N-(2-hydroxyethyl)morpholine (363 uL, 3 mmol) in anhydrous tetrahydrofuran (7 mL), under nitrogen, was added 1M sodium hexamethyldisilamide (3 mL, 3 mmol) in tetrahydrofuran at ambient temperature. The reaction mixture was stirred for 15 minutes, then the dithietane prepared as set forth in Step 1 of Example A-341 (636mg, 2 mmol) was added as a solid. The reaction mixture gradually became dark orange. After about 18 hours at ambient temperature, the reaction was quenched with saturated sodium bicarbonate solution (30 mL) and extracted twice with ethyl acetate (30 mL). The organic solutions were combined and washed with saturated NaCl solution (20 mL), then dried ( $\text{MgSO}_4$ ), filtered, and concentrated to an orange oil. The oil was taken up in methanol (10 mL) and reconcentrated to remove any remaining ethyl acetate. The oil was then taken up in methanol (5 mL) and anhydrous hydrazine (69 uL) was added. The reaction mixture was allowed to stir at ambient temperature 18 hours, then quenched with saturated sodium bicarbonate solution (30 mL) and extracted twice with ethyl acetate (30 mL). The organic solutions were combined and washed with water (20 mL) and saturated NaCl solution (20 mL), then dried ( $\text{MgSO}_4$ ), filtered, and concentrated to an orange semi-solid. The solid was triturated with acetonitrile (5 mL), collected by suction filtration, washed with acetonitrile and dried in-vacuo. Yield: off-white solid, 114 mg (14.8%); mp 198.9-199.9 °C;  $^1\text{H-NMR}$  ( $\text{DMSO-d}_6$ /300 MHz) 12.61 (br s, 1H), 8.41 (d, 2H), 7.52 (d, 2H), 7.38 (d, 2H), 7.21 (d, 2H), 4.33 (t, 2H), 3.54 (m, 4H), 2.70 (t, 2H), 2.44 (m, 4H); ESHRMS  $m/z$  385.1444 ( $\text{M}+\text{H}$ ,  $\text{C}_{20}\text{H}_{22}\text{ClN}_4\text{O}_2$  requires 385.1431).

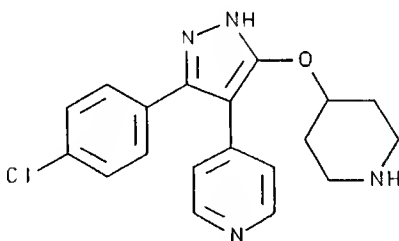
## Example A-441



5        The above compound was prepared in an analogous manner to that of Example A-440, starting with 4-hydroxy-N-t-boc piperidine. Recrystallized from acetone/methanol. Yield: white solid 263 mg (29%); mp 230.1-231.8 °C; <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>/300 MHz) 12.61 (br s, 1H), 8.42 (d, 2H), 7.52 (d, 2H), 7.38 (d, 2H), 7.20 (d, 2H), 4.88 (m, 1H), 3.52 (m, 2H), 3.30 (m, 2H), 1.93 (m, 2H), 1.65 (m, 2H), 1.39 (s, 9H); Anal. Calc'd for C<sub>24</sub>H<sub>27</sub>ClN<sub>4</sub>O<sub>3</sub>: C, 63.36; H, 5.98; N, 12.31; Found: C, 63.34; H, 5.97; N, 12.22.

15

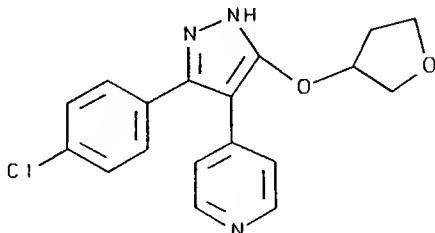
## Example A-442



20        Example A-441 (130 mg, 0.28 mmol) was treated with concentrated HCl (0.5 mL) in ethanol (5 mL) for two hours. The solvent was removed in-vacuo and the resulting residue dissolved in ethanol and reconcentrated twice. The resulting solid was triturated with  
25        acetonitrile to afford a white solid. Yield: 119 mg (91%) tri-hydrochloride salt; mp 220.6-222.1 °C; <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>/300 MHz) 13.25 (br s, 1H), 9.10 (br s, 2H), 8.67 (d, 2H), 7.75 (d, 2H), 7.60 (d, 2H), 7.50 (d, 2H), 5.04

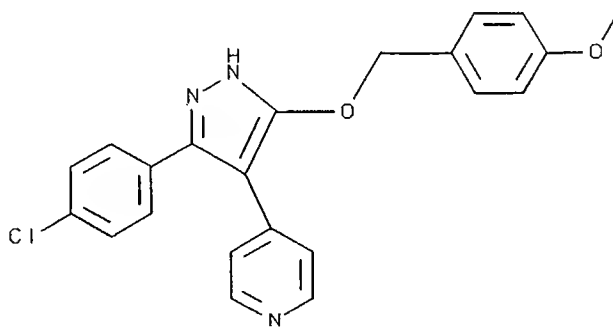
(m, 1H), 3.17 (br d, 4H), 2.21 (m, 2H), 2.03 (m, 2H);  
 Anal. Calc'd for  $C_{19}H_{19}ClN_4O \cdot 3 HCl$ : C, 49.16; H, 4.78; N, 12.07. Found: C, 49.24; H, 4.72; N, 12.02.

5

**Example A-443**

The above compound was prepared in a manner  
 10 analogous to Example A-440 starting with (+/-)-3-  
 hydroxytetrahydrofuran. Recrystallized from ethanol.  
 Yield: white crystalline solid, 57 mg (8%); mp >300 °C;  
<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>/300 MHz) 12.65 (br s, 1H), 8.42 (d, 2H),  
 7.52 (d, 2H), 7.38 (d, 2H), 7.18 (d, 2H), 5.28 (m, 1H),  
 15 3.86 (m, 2H), 3.82 (m, 1H), 3.75 (m, 1H), 2.26-2.01 (br  
 m, 2H); Anal. Calc'd for  $C_{18}H_{16}ClN_3O_2$ : C, 63.25; H, 4.72;  
 N, 12.29. Found: C, 63.12; H, 4.51; N, 12.31.

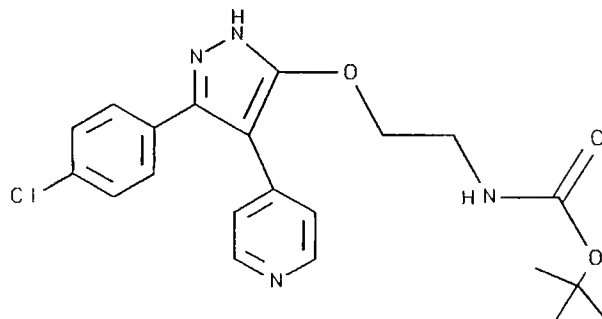
20

**Example A-444**

The above compound was prepared in a manner  
 analogous to Example A-440 starting with p-methoxybenzyl  
 25 alcohol. Yield: off-white solid, 252 mg (21%); mp =229.1-  
 229.2 °C; <sup>1</sup>H-NMR (acetone-d<sub>6</sub>/300 MHz) 11.62 (br s, 1H),  
 8.40 (br s, 2H), 7.76 (s, 2H), 7.39 (m, 4H), 7.30 (br s,  
 2H), 6.87 (d, 2H), 5.27 (s, 2H), 3.77 (s, 3H); Anal.

Calc'd for  $C_{22}H_{18}ClN_3O_2 \cdot 0.25 H_2O$ : C, 66.67; H, 4.70; N, 10.60. Found: C, 66.79 ; H, 4.95 ; N, 10.54.

### Example A-445

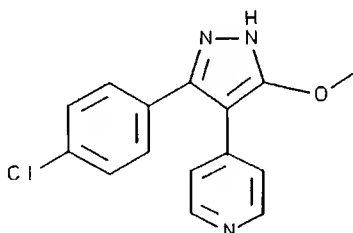


5

The above compound was prepared in a manner analogous to Example A-440 starting with N-tert-butoxycarbonyl-ethanolamine. Recrystallized from ethyl acetate/methanol. Yield: white solid, 75 mg (4 %); mp >300 °C;  $^1H$ -NMR (DMSO- $d_6$ /300 MHz) 12.60 (br s, 1H), 8.38 (d, 2H), 7.53 (d, 2H), 7.38 (d, 2H), 7.22 (d, 2H), 7.02 (t, 1H), 4.20 (t, 2H), 3.34 (m, 2H), 1.36 (s, 9H); ESHRMS  $m/z$  415.1551 (M+H,  $C_{21}H_{24}ClN_4O_3$  requires 415.1537)

15

### Example A-446

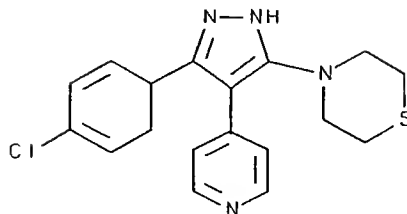


The above compound was prepared in a manner analogous to Example A-440 starting with methanol. Yield: off-white solid, 119 mg (14 %); mp = 265.3-265.3 °C;  $^1H$ -NMR (DMSO- $d_6$ /300 MHz) 12.61 (br s, 1H), 8.41 (d, 2H), 7.52 (d, 2H), 7.38 (d, 2H), 7.17 (d, 2H), 3.90 (s, 3H); ESHRMS  $m/z$  286.0766 (M+H,  $C_{15}H_{13}ClN_3O$  requires 286.0747); Anal. Calc'd for  $C_{15}H_{12}ClN_3O \cdot 0.25 H_2O$ : C, 62.08; H, 4.34; N, 14.48. Found: C, 62.24; H, 4.11; N,

20

25

14.16.

**Example A-447**

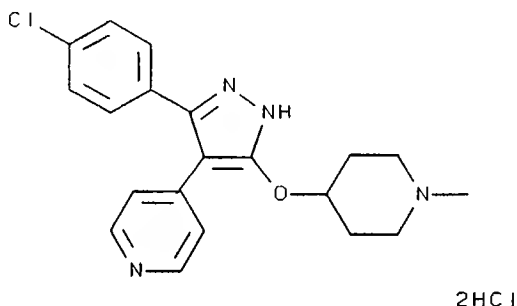
5

To the dithietane of Step 1 of Example A-341 (638 mg, 2 mmol) in toluene (15 mL) was added thiomorpholine (800 uL, 8 uL). The reaction mixture was heated to reflux for 6 hours, then cooled to room temperature and diluted with toluene (20 mL). The reaction mixture was then extracted twice with water (20 mL) and brine (20 mL). The organic solution was dried (MgSO<sub>4</sub>), filtered, and concentrated to an oil. Hexane was added to the residue and heated to reflux, then decanted. The oil became semi-solid. The semi-solid was dissolved in tetrahydrofuran (10 mL) and potassium t-butoxide 1M in tetrahydrofuran (2 mL, 2 mmol) was added. This was followed by iodomethane (125 uL, 2 mmol). The reaction was stirred at room temperature for 1 hour, then quenched with water (20 mL). The reaction mixture was extracted with ethyl acetate (2 x 30 mL). The organic layers were pooled, washed with brine (20 mL) and dried (MgSO<sub>4</sub>). Filtration and concentration produced an oil which was chased once with toluene to remove any ethyl acetate. The residue was dissolved in ethanol (10 mL) and hydrazine hydrate (97 uL, 2 mmol) was added. The reaction mixture was stirred at room temperature for 4 hours then partitioned between ethyl acetate and saturated sodium bicarbonate solution (30 mL each). The layers were separated and the aqueous layer extracted again with ethyl acetate (30 mL). The combined organic

layers were washed with brine (20 mL) and dried (MgSO<sub>4</sub>). Filtration and concentration produced an orange residue which was triturated with acetonitrile to generate a tan solid. Yield: 295 mg (43%); mp >300 °C; <sup>1</sup>H NMR (DMSO-  
 5 d<sub>6</sub>/300 MHz) 12.70 (br s, 1H), 8.47 (d, 2H), 7.46 (d, 2H), 7.26 (m, 4H), 3.13 (m, 4H), 2.62 (m, 4H); ESHRMS m/z 357.0942 (M+H, C<sub>18</sub>H<sub>18</sub>ClN<sub>4</sub>S requires 357.0941); Anal. Calc'd for C<sub>18</sub>H<sub>17</sub>ClN<sub>4</sub>S: C, 60.58; H, 4.80; N, 15.70. Found: C, 60.32; H, 4.96; N, 15.60.

10

**Example A-448**

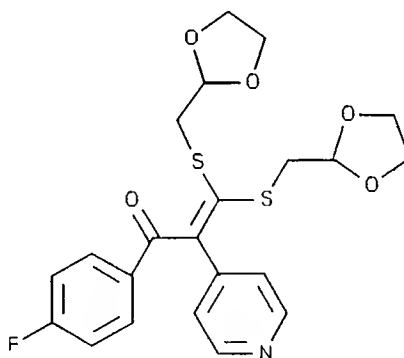


15            3-(4-chlorophenyl)-5-[(1-methylpiperidin-4-yl)-oxy]-  
 4-pyridin-4-yl-1H-pyrazole

The compound of Example A-441 (455 mg, 1.5 mmol) was combined with 98% formic acid (6 mL) and heated to 100  
 20 °C. After three hours, 37% formaldehyde (1.22 mL, 15 mmol) was added and the reaction was heated for an additional five hours at 100 °C. The reaction mixture was allowed to cool to room temperature and filtered. The solution was diluted with water (15 mL) and extracted  
 25 once with ethyl acetate (30 mL). The aqueous solution was then basified with 2.5 N sodium hydroxide to pH 8. The cloudy mixture was then extracted twice with 1:1 tetrahydrofuran:ethyl acetate (30 mL). The organic layers were pooled and washed once with brine (25 mL),  
 30 dried (MgSO<sub>4</sub>), filtered and concentrated to an oil which solidified on standing. The solid was triturated with

acetonitrile and collected by suction filtration. The solid was suspended in ethanol:water 2:1 (15 mL) and 1 mL of concentrated HCl was added. The solution was allowed to stir at room temperature for one hour, then  
 5 filtered and concentrated. The residue was combined with ethanol (10 mL) and reconcentrated twice. The resulting solid was triturated with acetonitrile (10 mL) containing a small amount of ethanol (0.5 mL) to remove some colored impurities. The solid was collected by suction  
 10 filtration, washed with acetonitrile and dried in-vacuo. Yield: 490 mg (88 %); mp 255.9-256.8 °C; <sup>1</sup>H NMR (D<sub>2</sub>O/DMSO-d<sub>6</sub>/NaOD/300 MHz) 7.93 (d, 2H), 7.09 (s, 4H), 7.00 (d, 2H), 4.42 (m, 1H), 2.26 (br m, 2H,) 2.12 (br m, 2H), 1.92 (s, 3H), 1.68 (br m, 2 H), 1.57 (br m, 2H);  
 15 ESLRMS m/z 369 (M+H).

#### Example A-449

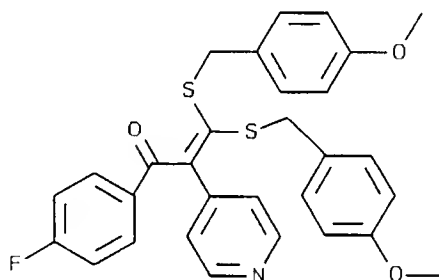


20 To the compound of Example C-1, infra, (4'-fluoro-1-(4-pyridyl)acetophenone, 14.0 g, 0.065 mol) in anhydrous tetrahydrofuran (200 mL) was added dropwise potassium t-butoxide (1M in tetrahydrofuran, 150 mL). The mixture  
 25 was stirred 30 minutes. Carbon disulfide (4.2 mL, 0.07 mol) in tetrahydrofuran (25 mL) was added dropwise and stirred 15 minutes. 2-Bromomethyl-1,3-dioxolane (25.0 g, 0.15 mol) in tetrahydrofuran (25 mL) was added dropwise and contents were refluxed 10 hours. The mixture was  
 30 allowed to cool and partitioned between ethyl acetate and

water. The ethyl acetate layer was dried over  $\text{MgSO}_4$  and concentrated in vacuo leaving a red oil (29.3 g).

Chromatography on silica gel eluting with 25% ethyl acetate/hexanes gave the desired compound as a red oil,  
 5 (5.5 g, 18% yield).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ) 8.62-8.52 (m, 2H); 8.07-7.95 (m, 2H); 7.48-7.40 (m, 2H); 7.20-7.05 (m, 2H); 5.15-5.05 (m, 1H); 4.98-4.90 (m, 1H); 4.00-3.77 (m, 8H); 3.08 (d,  $J = 6$  Hz, 2H); 3.03 (d,  $J = 6$  Hz, 2H); ESHRMS  $m/z$  464.0966 ( $\text{M}+\text{H}$ ,  $\text{C}_{22}\text{H}_{23}\text{FNO}_5\text{S}_2$  requires 464.1001); Anal.  
 10 Calc'd for:  $\text{C}_{22}\text{H}_{22}\text{FNO}_5\text{S}_2$  (0.1  $\text{H}_2\text{O}$ ): C, 56.79; H, 4.81; N, 3.01. Found: C, 56.45; H, 4.71; N, 3.02.

#### Example A-450

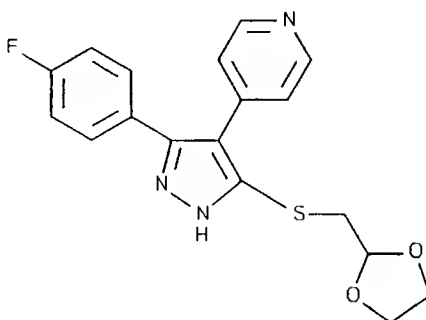


To the compound of Example C-1, *infra*, (4'-fluoro-1-(4-pyridyl)acetophenone, 7.0 g, 0.0325 mol) in anhydrous tetrahydrofuran (200 mL) was added dropwise potassium *t*-butoxide (1M in tetrahydrofuran, 75 mL). The mixture was  
 20 stirred 30 minutes. Carbon disulfide (2.1 mL, 0.035 mol) in tetrahydrofuran (25 mL) was added dropwise and stirred 15 minutes. 4-Methoxybenzyl chloride (10.2 mL, 0.075 mol) in tetrahydrofuran (10 mL) was added dropwise and  
 25 contents were stirred overnight. The contents were partitioned between ethyl acetate and water. The ethyl acetate layer was dried over  $\text{MgSO}_4$  and concentrated in vacuo leaving a red oil (19.1 g). Chromatography on silica gel eluting with 25% ethyl acetate/hexanes gave  
 30 the desired as a white solid (11.8 g, 68% yield). Recrystallization from ethyl acetate/hexanes gave the desired as colorless crystals: mp 118.5 - 120.6  $^{\circ}\text{C}$ ;  $^1\text{H}$

431

NMR (CDCl<sub>3</sub>) 8.43 (d, *J* = 7 Hz, 2H); 7.62-7.52 (m, 2H);  
 7.20-6.72 (m, 12H); 3.98 (d, *J* = 6 Hz, 4H); 3.83 (s, 3H);  
 3.81 (s, 3H); ESHRMS *m/z* 532.1408 (M+H, C<sub>30</sub>H<sub>27</sub>FNO<sub>3</sub>S<sub>2</sub>  
 requires 532.1416); Anal. Calc'd for: C<sub>30</sub>H<sub>26</sub>FNO<sub>3</sub>S<sub>2</sub> (0.5  
 5 H<sub>2</sub>O): C, 66.65; H, 5.03; N, 2.59. Found: C, 66.34; H,  
 4.96; N, 2.55.

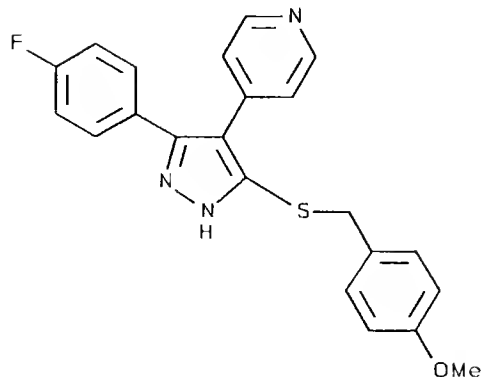
### Example A-451



10

The compound of Example A-449 (4.0 g, 9.2 mmol) and  
 hydrazine monohydrate (2.2 mL, 46 mmol) were refluxed in  
 ethanol (100 mL) for three hours. The mixture was  
 15 allowed to cool and stand overnight. A yellow  
 precipitate was filtered to give the desired product as a  
 yellow solid, (1.34 g, 41% yield); mp 202.1-205.4°C; <sup>1</sup>H  
 NMR (DMSO-*d*<sub>6</sub>) 13.5 (br s, 1H); 8.55-8.45 (m, 2H); 7.40-  
 7.12 (m, 6H); 5.01 (s, 1H); 3.92-3.70 (m, 4H); 3.13 (s,  
 20 2H); ESHRMS *m/z* 358.1025 (M+H, C<sub>18</sub>H<sub>17</sub>FN<sub>3</sub>O<sub>2</sub>S requires  
 358.1025); Anal. Calc'd for: C<sub>18</sub>H<sub>16</sub>FN<sub>3</sub>O<sub>2</sub>S: C, 60.49; H,  
 4.51; N, 11.76. Found: C, 60.26; H, 4.55 N, 11.87.

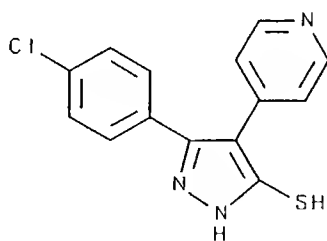
## Example A-452



5        The above compound was prepared similarly to the compound of Example A-451 starting with the compound prepared in Example A-450. The desired product was obtained as a white solid (2.15 g, 49% yield); mp 214.7-215.8 °C; <sup>1</sup>H NMR (DMSO-d<sub>6</sub> + approx. 10%TFA) 8.70 (d, 2H);  
 10    7.60 (d, 2H); 7.42-7.38 (m, 2H); 7.30-7.20 (m, 2H); 6.70 (d, 2H); 4.10 (s, 2H); 3.68 (s, 3H); ESHRMS m/z 392.1225 (M+H, C<sub>22</sub>H<sub>19</sub>FN<sub>3</sub>OS requires 392.1232); Anal. Calc'd for: C<sub>22</sub>H<sub>18</sub>FN<sub>3</sub>OS: C, 67.50; H, 4.63; N, 10.73. Found: C, 67.46; H, 4.67 N, 10.77.

15

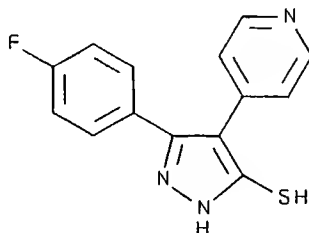
## Example A-453



20        The compound prepared in step 1 of Example A-341 (50 g, 0.156 mol) and anhydrous hydrazine (25 mL, 0.8 mol) were refluxed in ethanol (500 mL) for five hours. The mixture was allowed to cool and the precipitate filtered to afford the desired product as a yellow-orange solid  
 25    (21.8 g). The filtrate was diluted with water (200 mL) and a second crop was obtained as a yellow-orange solid

(18.0 g). The pH of the filtrate was adjusted to pH 8 with 3N HCl and the precipitated solid filtered to give more desired as a yellow-orange solid (2.0 g). The product was obtained in 93% yield. mp 266.3-268.9°C; <sup>1</sup>H NMR (DMSO-d<sub>6</sub>) 13.80 (br, 1H); 12.20 (br s, 1H); 8.32 (s, 4H); 7.50-7.30 (m, 4H); ESHRMS m/z 288.0358 (M+H, C<sub>14</sub>H<sub>11</sub>ClN<sub>3</sub>S requires 288.0362); Anal. Calc'd for: C<sub>14</sub>H<sub>10</sub>ClN<sub>3</sub>S (0.4 H<sub>2</sub>O): C, 57.01; H, 3.69; N, 14.25. Found: C, 56.95; H, 3.50 N, 14.14.

#### Example A-454



The above compound was prepared similarly to the compound of Example A-453. mp 261.3-263.9°C; <sup>1</sup>H NMR (DMSO-d<sub>6</sub>) 11.55 (br s, 1H); 8.25-8.13 (m, 2H); 7.61-7.50 (m, 2H); 7.36-7.20 (m, 2H); 7.19-7.05 (m, 2H); ESHRMS m/z 272.0691 (M+H, C<sub>14</sub>H<sub>11</sub>FN<sub>3</sub>S requires 272.0657); Anal. Calc'd for: C<sub>14</sub>H<sub>10</sub>FN<sub>3</sub>S (0.25 H<sub>2</sub>O): C, 60.97; H, 3.84; N, 15.24. Found: C, 61.05; H, 3.64 N, 15.12.

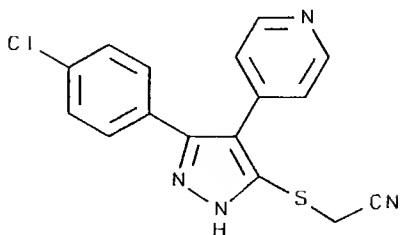
#### Example A-455

To the compound prepared in Example A-453 (100 mg, 0.35 mmol) in methanol (2 mL) was added 0.5 M sodium methoxide (0.7 mL, 0.35 mmol). The mixture was stirred for 15 minutes and filtered to remove some small particles. The filtrate was concentrated in vacuo, dissolved in water and concentrated in vacuo leaving the desired product as a white solid. <sup>1</sup>H NMR (DMSO-d<sub>6</sub>) 11.60 (br s, 1H); 8.20 (d, 2H); 7.60-7.50 (m, 2H); 7.40-7.20 (m, 4H); Anal. Calc'd for: C<sub>14</sub>H<sub>9</sub>ClN<sub>3</sub>NaS (2.5 H<sub>2</sub>O): C,

47.40; H, 3.98; N, 11.84. Found: C, 47.39; H, 3.33; N, 11.50.

### Example A-456

5

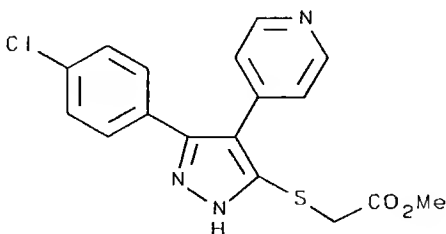


[3-(4-chlorophenyl)-4-pyridin-4-yl-1H-pyrazole-5-yl]thio]acetonitrile

10 To the compound prepared in Example A-453 (584 mg, 2.0 mmol) and bromoacetonitrile (140  $\mu$ l, 2.0 mmol) in dimethylformamide (5 mL) was added anhydrous potassium carbonate (276 mg, 2.0 mmol). The contents were stirred overnight, then partitioned between ethyl acetate and  
15 water. The ethyl acetate layer was dried over  $\text{MgSO}_4$  and concentrated in vacuo leaving a tan solid. The solid was triturated with methanol and filtered to give the desired as a off-white solid (369 mg, 56% yield). mp 230.0-230.5°C;  $^1\text{H}$  NMR ( $\text{DMSO}-d_6$ ) 13.90 (br s, 1H); 8.58 (d, 2H);  
20 7.60-7.13 (m, 6H); 4.10 (s, 2H); ESHRMS  $m/z$  327.0482 ( $\text{M}+\text{H}$ ,  $\text{C}_{16}\text{H}_{12}\text{ClN}_4\text{S}$  requires 327.0471); Anal. Calc'd for:  $\text{C}_{16}\text{H}_{11}\text{ClN}_4\text{S}$  ( $0.3 \text{ H}_2\text{O}$ ): C, 57.85, H, 3.52; N, 16.87. Found C, 57.88; H, 3.31; N, 16.77.

25

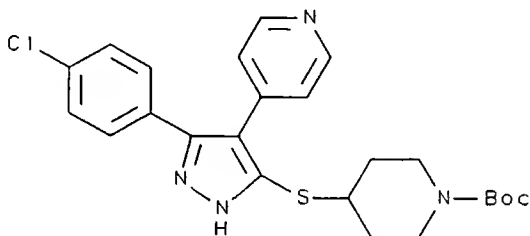
### Example A-457



The above compound was prepared similarly to the

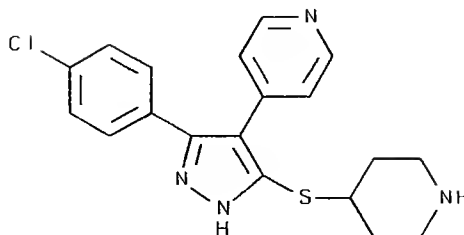
compound of Example A-456 except that when the contents were partitioned between ethyl acetate and water, an insoluble solid was filtered to give the desired product as a white solid (2.16 g). A second crop (1.68 g) of  
 5 desired product gave a total yield of 61%. mp 192.8-195.2°C; <sup>1</sup>H NMR (DMSO-d<sub>6</sub> + approximately 10%TFA) 9.80 (d, 2H); 7.80 (d, 2H); 7.52-7.34 (m, 4H); 3.92 (s, 2H); 3.57 (s, 3H); ESHRMS m/z 360.05735 (M+H, C<sub>17</sub>H<sub>14</sub>ClN<sub>3</sub>O<sub>2</sub>S requires 360.05732); Anal. Calc'd for: C<sub>17</sub>H<sub>14</sub>ClN<sub>3</sub>O<sub>2</sub>S (0.25 H<sub>2</sub>O): C, 56.05, H, 4.01; N, 11.53. Found C, 56.10; H, 3.72; N, 11.51.

#### Example A-458



The compound prepared in Example A-453 (1.2 g, 4.2 mmol), potassium carbonate (630 mg, 4.6 mmol), N-tert-butoxycarbonyl-4-bromo piperidine (1.2 g, 4.5 mmol) were  
 20 heated in dimethylformamide (15 mL) at 105 °C for three hours. Contents were allowed to cool and partitioned between ethyl acetate and water. The ethyl acetate layer was dried over MgSO<sub>4</sub> and concentrated in vacuo. The  
 25 residue was triturated with ethyl acetate and filtered to give the desired as a white solid (1.2 g, 61% yield). mp 220.9-221.0°C; <sup>1</sup>H NMR (DMSO-d<sub>6</sub>) 13.70 (br, 1H); 8.60-8.50 (m, 2H); 7.58-7.10 (m, 6H); 3.80-3.60 (m, 2H); 3.40-3.20 (m, 1H); 3.00-2.63 (m, 2H); 2.00-1.53 (m, 2H); 1.50-1.05 (m, 2H); 1.40 (s, 9H); ESHRMS m/z 471.1605 (M+H, C<sub>24</sub>H<sub>28</sub>ClN<sub>4</sub>OS requires 471.1622); Anal. Calc'd for: C<sub>24</sub>H<sub>27</sub>ClN<sub>4</sub>OS (0.5 H<sub>2</sub>O): C, 60.05; H, 5.88; N, 11.67. Found: C, 60.04; H, 5.57; N, 11.31.

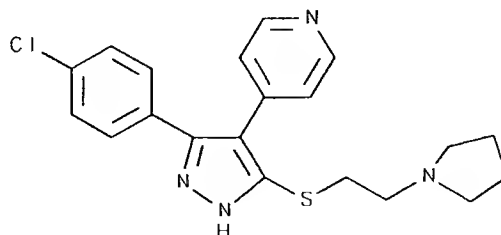
## Example A-459



5            3-(4-chlorophenyl)-5-[(piperidin-4-yl)-thio]-4-pyridin-4-yl-1H-pyrazole

The compound prepared in Example A-458 (5.0 g, 11 mmol), and TFA (30 mL) were mixed in methylene chloride  
 10 (50 mL) and stirred overnight. The mixture was concentrated in vacuo leaving a pale yellow oil which was dissolved in water. The pH was adjusted with 2.5 N sodium hydroxide to pH 9, precipitating a white solid which was filtered to give the desired product as a white  
 15 solid (3.7 g, 93% yield). mp 211.1-211.2°C; <sup>1</sup>H NMR (DMSO-d<sub>6</sub>) 13.80 (br, 1H); 8.55 (d, 2H); 8.40 (br, 1H); 7.50-7.15 (m, 6H); 3.50-3.00 (m, 3H); 3.00-2.80 (m, 2H); 2.05-1.80 (m, 2H); 1.65-1.42 (m, 2H); ESHRMS m/z 371.1103 (M+H, C<sub>19</sub>H<sub>20</sub>ClN<sub>4</sub>S requires 371.1097); Anal. Calc'd for: C<sub>19</sub>H<sub>19</sub>ClN<sub>4</sub>S (H<sub>2</sub>O): C, 58.68; H, 5.44; N, 14.41. Found: C, 58.86; H, 5.28; N, 14.25.  
 20

## Example A-460

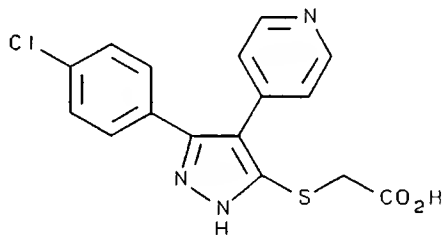


25

To 1-(2-chloroethyl)pyrrolidine hydrochloride (306 mg, 1.8 mmol) in methanol (10 mL) was added 0.5 M sodium methoxide (7.0 mL, 3.6 mmol). The mixture was stirred 10

minutes and the compound of Example A-453 (500 mg, 1.8 mmol) added. The contents were refluxed one hour, allowed to cool and partitioned between ethyl acetate and water. The ethyl acetate layer was dried over  $\text{MgSO}_4$  and concentrated in vacuo leaving a light amber solid. The solid was recrystallized from methanol (15 mL) to give the desired product as a white solid (213 mg, 33% yield). mp 189.9-190.1°C;  $^1\text{H}$  NMR ( $\text{DMSO}-d_6$ ) 13.65 (br, 1H); 8.52 (d, 2H); 7.42 (d, 2H); 7.38-7.10 (m, 4H); 3.10-2.93 (m, 2H); 2.63-2.51 (m, 2H); 2.38 (br s, 4H); 1.70-1.52 (m, 4H); ESHRMS  $m/z$  385.1262 ( $\text{M}+\text{H}$ ,  $\text{C}_{20}\text{H}_{22}\text{ClN}_4\text{S}$  requires 385.1254); Anal. Calc'd for:  $\text{C}_{20}\text{H}_{21}\text{ClN}_4\text{S}$ : C, 62.41, H, 5.50; N, 14.56. Found C, 62.22; H, 5.62; N, 14.48.

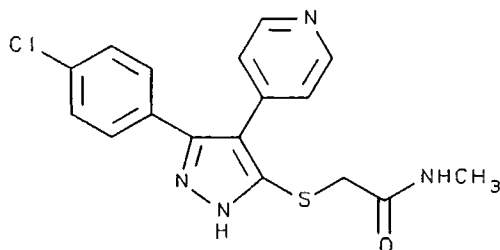
#### Example A-461



Method A: The compound prepared in Example A-457 (1.3 g, 3.6 mmol) in methanol (10 mL), 2.5N sodium hydroxide (4 mL) and water (10 mL) were stirred overnight. The mixture was concentrated in vacuo to remove the methanol and the aqueous solution left was made acidic to pH 6 with 3N HCl, precipitating a solid. The solid was extracted into ethyl acetate, dried over  $\text{MgSO}_4$  and concentrated in vacuo leaving light tan crystals (205 mg). Brine was added to the aqueous layer precipitating more solid. The solid did not extract into ethyl acetate, but was filtered to give more desired product as a light tan powder (529 mg). Total yield was 61% yield.  $^1\text{H}$  NMR ( $\text{DMSO}-d_6 + 10\%\text{TFA}$ ) 8.80 (d, 2H); 7.83 (d, 2H); 7.55-7.35 (m, 4H); 3.87 (s, 2H).

Method B: The compound prepared in Example A-457 (3.8 g, 11 mmol) and 3N HCl (30 mL) were refluxed for three hours. The mixture was allowed to cool and concentrated in vacuo. The residue was mixed with CH<sub>3</sub>CN (50 mL). Upon standing overnight, pale yellow crystals grew and were filtered to give the desired product as the HCl salt (2.9 g, 69% yield). <sup>1</sup>H NMR (DMSO-d<sub>6</sub>) 8.79 (d, 2H); 7.75 (d, 2H); 7.51-7.38 (m, 4H); 3.88 (s, 2H); ESHRMS m/z 346.0435 (M+H, C<sub>17</sub>H<sub>16</sub>ClN<sub>4</sub>OS requires 346.0417); Anal. Calc'd for: C<sub>16</sub>H<sub>12</sub>ClN<sub>3</sub>O<sub>2</sub>S (HCl, 0.5 H<sub>2</sub>O): C, 49.12; H, 3.61; N, 10.74. Found: C, 49.36; H, 3.48; N, 10.72.

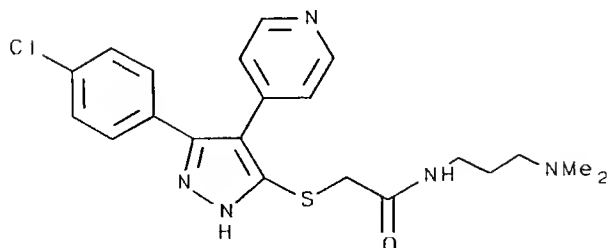
#### Example A-462



The compound prepared in Example A-457 (400 mg, 11 mmol) and a 2M solution of methyl amine in tetrahydrofuran (25 mL) were refluxed for three hours. The mixture was stirred overnight at room temperature before filtering to give the desired as a light amber solid (335 mg, 85 % yield). mp 284.0-288.4°C; <sup>1</sup>H NMR (DMSO-d<sub>6</sub>) 13.58 (br, 1H); 8.60-8.45 (m, 2H); 7.98 (br s, 1H); 7.55-7.12 (m, 6H); 3.60 (s, 2H); 2.46 (s, 3H); ESHRMS m/z 359.0733 (M+H, C<sub>17</sub>H<sub>16</sub>ClN<sub>4</sub>OS requires 359.0745); Anal. Calc'd for: C<sub>17</sub>H<sub>15</sub>ClN<sub>4</sub>OS: C, 56.90; H, 4.21; N, 15.61. Found: C, 56.74; H, 4.11; N, 15.17.

439

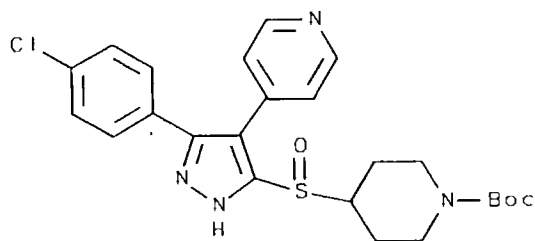
## Example A-463



5        The compound prepared in Example A-457 (415 mg, 12 mmol) and N, N-dimethylaminopropylamine were refluxed in methanol (25 mL) for three hours. The mixture was stirred overnight at room temperature before concentrating in vacuo leaving a solid. The solid was  
10    trituated with ethyl acetate and filtered to give the desired as a white solid (256 mg, 50 % yield). mp 168.8-169.5°C; <sup>1</sup>H NMR (DMSO-d<sub>6</sub>) 13.80 (br, 1H); 8.55-8.50 (m 2H); 8.02 (t, 1H); 7.50-7.40 (m, 6H); 3.61 (s, 2H); 3.30-2.98 (m, 2H); 2.14-2.10 (m, 2H); 2.04 (s, 6H); 1.50-1.40  
15    (m, 2H); ESHRMS m/z 430.1472 (M+H, C<sub>21</sub>H<sub>25</sub>ClN<sub>12</sub>OS requires 430.1468); Anal. Calc'd for: C<sub>21</sub>H<sub>24</sub>ClN<sub>5</sub>OS (0.5 H<sub>2</sub>O): C, 57.46; H, 5.74; N, 15.95. Found: C, 57.71; H, 5.56; N, 16.12.

20

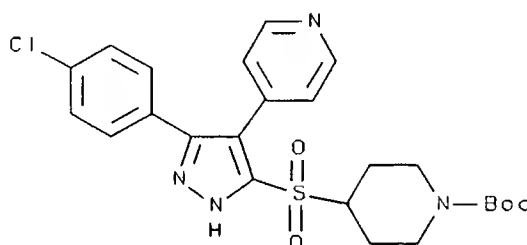
## Example A-464



25        To the compound prepared in Example A-458 (1.0 g, 2.1 mmol) in methylene chloride (25 mL) was added meta-chloroperbenzoic acid (425 mg, 2.1 mmol). The mixture was stirred 15 minutes and chromatographed on silica gel (20 g) eluting with ethyl acetate. The desired product precipitated out of the ethyl acetate elutant upon

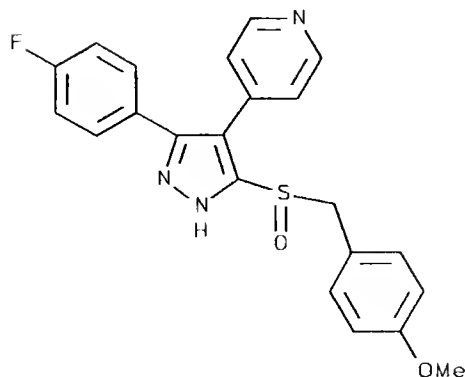
standing and was filtered to give the desired product as a white solid (958 mg, 93% yield). mp 215.8-215.9°C; <sup>1</sup>H NMR (DMSO-d<sub>6</sub>) 14.34 (br s, 1H); 8.57-8.54 (m, 2H); 7.51-7.25 (m, 6H); 4.00-3.82 (m, 2H); 3.60-3.40 (m, 1H); 2.85-2.70 (m, 2H); 2.10-1.95 (m, 1H); 1.56-1.10 (m, 3H); 1.36 (s, 9H); ESHRMS m/z 487.1580 (M+H, C<sub>17</sub>H<sub>16</sub>ClN<sub>4</sub>O<sub>3</sub>S requires 487.1571); Anal. Calc'd for: C<sub>24</sub>H<sub>27</sub>ClN<sub>12</sub>O<sub>3</sub>S: C, 59.19; H, 5.59; N, 11.50. Found: C, 59.00; H, 5.76; N, 11.46.

### Example A-465



To the compound prepared in Example A-458 (320 mg, 0.68 mmol) in ethanol (5 mL) was added an aqueous solution of potassium peroxymonosulfate (420 mg, 0.68 mmol). The mixture was stirred two hours and extracted into ethyl acetate which was dried over MgSO<sub>4</sub> and concentrated in vacuo leaving a white solid. The solid was triturated with methanol and filtered to give the desired as a white solid (90 mg, 26% yield). mp 228.0-230.8°C; <sup>1</sup>H NMR (DMSO-d<sub>6</sub>) 8.61 (d, 2H); 7.48 (d, 2H); 7.31-7.20 (m, 4H); 4.05-3.90 (m, 2H); 3.54-3.35 (m, 1H); 2.85-2.60 (m, 2H); 1.92-1.80 (m, 2H); 1.48-1.25 (m, 2H); 1.32 (s, 9H); ESHRMS m/z 503.1541 (M+H, C<sub>24</sub>H<sub>27</sub>ClN<sub>4</sub>O<sub>4</sub>S requires 503.1520); Anal. Calc'd for: C<sub>24</sub>H<sub>27</sub>ClN<sub>4</sub>O<sub>4</sub>S (H<sub>2</sub>O): C, 56.30; H, 5.51; N, 10.94. Found: C, 56.41; H, 5.78; N, 10.54.

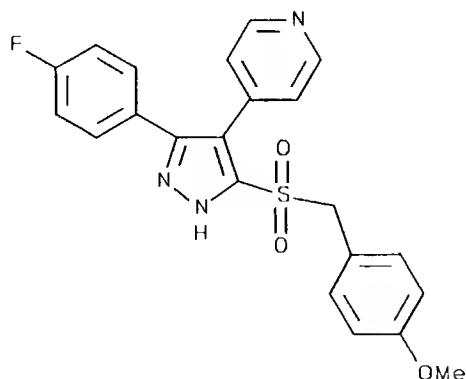
## Example A-466



5        The above compound was prepared similarly to the compound of Example A-464. After chromatography the solid obtained was recrystallized from CH<sub>3</sub>CN to give the desired product as white crystals (64 mg, 33% yield). mp 189.5-189.5°C; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) 14.28 (br s, 1H); 8.50 (d, 2H); 7.40-7.20 (m, 4H); 7.20-7.05 (m, 4H); 6.85 (d, 2H); 4.41 (s, 2H); 3.70 (s, 3H); ESHRMS *m/z* 408.1168 (M+H, C<sub>22</sub>H<sub>19</sub>FN<sub>3</sub>O<sub>2</sub>S requires 408.1182); Anal. Calc'd for: C<sub>22</sub>H<sub>18</sub>FN<sub>3</sub>O<sub>2</sub>S: C, 64.85; H, 4.45; N, 10.31. Found: C, 64.44; H, 4.34; N, 10.70.

15

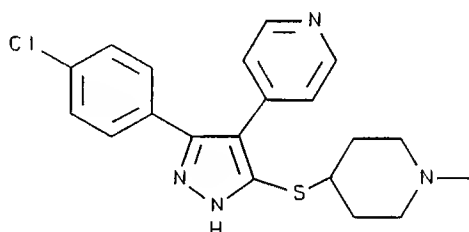
## Example A-467



20        To the compound prepared in Example A-466 (1.2 g, 2.5 mmol) in methylene chloride (50 mL) was added *meta*-chloroperbenzoic acid (1.0 g, 5.0 mmol). The mixture was stirred 1.5 hours and filtered a white solid (620 mg)

which was inorganic salts. The filtrate was chromatographed on silica gel (20 g) eluting with ethyl acetate to give the desired product as a white solid (98 mg, 9% yield). mp 241.9-242.0°C; <sup>1</sup>H NMR (DMSO-d<sub>6</sub>) 8.48-8.40 (m, 2H); 7.33-6.80 (m, 10H); 4.55 (s, 2H); 3.72 (s, 3H); ESHRMS m/z 424.1143 (M+H, C<sub>24</sub>H<sub>27</sub>ClN<sub>4</sub>O<sub>4</sub>S requires 424.1131); Anal. Calc'd for: C<sub>22</sub>H<sub>18</sub>FN<sub>3</sub>O<sub>3</sub>S: C, 62.40; H, 4.28; N, 9.92. Found: C, 62.14; H, 4.42; N, 9.68.

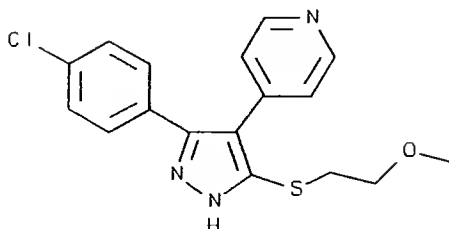
#### Example A-468



3-(4-chlorophenyl)-5-[(1-methylpiperidin-4-yl)-thio]-4-pyridin-4-yl-1H-pyrazole

The compound prepared in Example A-458 (5.0 g, 0.01 mol) and formic acid (96%, 7 mL) were heated at 100 °C for one hour. The mixture was allowed to cool to about 50 °C and formaldehyde (37%, 13 mL) was added. The contents were heated at 80 °C for two hours. The contents were allowed to cool, diluted with water (200 mL) and made basic to pH 11 with 2.5N sodium hydroxide, precipitating a white solid. The solid was filtered and recrystallized from methanol to give the desired as a white solid (174 mg, 33% yield). mp 227.7-227.7°C; <sup>1</sup>H NMR (DMSO-d<sub>6</sub>) 13.70 (br s, 1H); 8.56-8.48 (m, 2H); 7.50-7.15 (m, 6H); 3.10-2.92 (m, 1H); 2.63-2.50 (m, 2H); 2.05 (s, 3H); 1.95-1.65 (m, 4H); 1.50-1.30 (m, 2H); ESHRMS m/z 385.1233 (M+H, C<sub>20</sub>H<sub>22</sub>ClN<sub>4</sub>S requires 385.1254); Anal. Calc'd for: C<sub>20</sub>H<sub>21</sub>ClN<sub>4</sub>S: C, 62.41; H, 5.50; N, 14.56. Found: C, 62.40; H, 5.80; N, 14.61.

## Example A-469

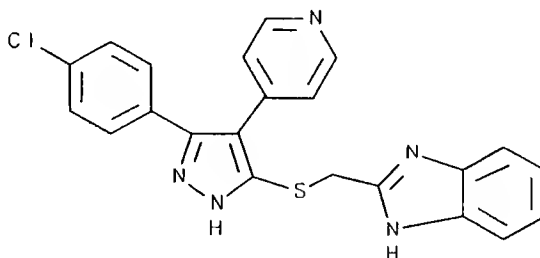


5            3-(4-chlorophenyl)-5-[(2-methoxyethyl)-thio]-4-pyridin-4-yl-1H-pyrazole

The above compound was prepared similarly to the compound of Example A-456 using bromoethyl methyl ether except contents were heated at 70 °C for one hour before partitioning between ethyl acetate and water. The crude product was recrystallized from methanol/ethyl acetate to give the desired product as a white solid (210 mg, 35% yield). mp 189.2-190.2°C; <sup>1</sup>H NMR (DMSO-d<sub>6</sub>) 8.60-8.45 (m, 2H); 7.60-7.10 (m, 6H); 3.60-2.85 (m, 7H); ESHRMS m/z 346.0799) M+H, C<sub>17</sub>H<sub>17</sub>ClN<sub>3</sub>OS requires 346.0781); Anal. Calc'd for: C<sub>17</sub>H<sub>16</sub>ClN<sub>3</sub>OS (H<sub>2</sub>O): C, 58.73; H, 4.70; N, 12.09. Found: C, 58.67; H, 4.86; N, 12.03.

20

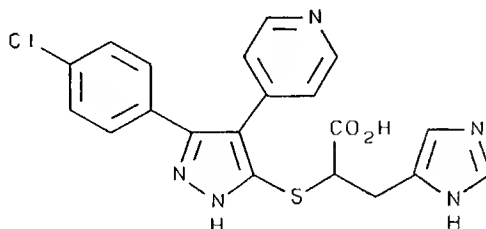
## Example A-470



The above compound was prepared similarly to the compound of Example A-456 using 2-chloromethylbenzimidazole except contents were heated at 70 °C for one hour before partitioning between ethyl acetate and water. An insoluble solid was filtered from the two layers and triturated with methanol to give the

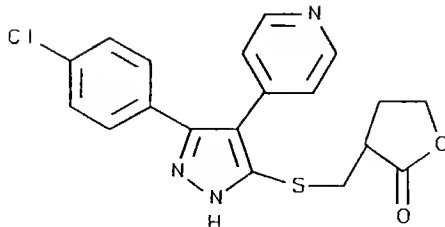
desired product as a light amber solid (292 mg, 40% yield). mp 257.7-257.7°C; <sup>1</sup>H NMR (DMSO-d<sub>6</sub>) 13.75 (br s, 1H); 12.30 (br s, 1H); 8.55-8.30 (m, 2H); 7.65-6.90 (m, 10H); 4.40 (br s, 2H); ESHRMS m/z 418.0895 (M+H, C<sub>22</sub>H<sub>17</sub>ClN<sub>5</sub>S requires 418.0893); Anal. Calc'd for: C<sub>22</sub>H<sub>16</sub>ClN<sub>5</sub>S (0.75 H<sub>2</sub>O): C, 61.25; H, 4.09; N, 16.23. Found: C, 61.27; H, 3.90; N, 15.92.

#### Example A-471



The above compound was prepared similarly to the compound of Example A-456 using DL- $\alpha$ -bromo- $\beta$ -(5-imidazolyl)propionic acid except the mixture was heated at 70 °C for one hour. The mixture contained an insoluble solid which was diluted with water and the pH was adjusted with 3N HCl to pH 7. The mixture was filtered and triturated with methanol to give the desired product as a white solid (1.5 g, 81% yield). mp 163.0-165.5°C; <sup>1</sup>H NMR (DMSO-d<sub>6</sub> + approx. 10%TFA) 8.92 (d, 1H); 8.83-8.75 (m, 2H); 7.80 (d, 2H); 7.55-7.30 (m, 5H); 4.20-4.05 (m, 1H); 3.25-3.00 (m, 2H). ESHRMS m/z 426.0799 (M+H, C<sub>20</sub>H<sub>17</sub>ClN<sub>5</sub>O<sub>2</sub>S requires 426.0791); Anal. Calc'd for: C<sub>20</sub>H<sub>16</sub>ClN<sub>5</sub>O<sub>2</sub>S (1.8 H<sub>2</sub>O): C, 52.41 H, 4.31; N, 15.28. Found: C, 52.68; H, 4.58; N, 15.37.

## Example A-472

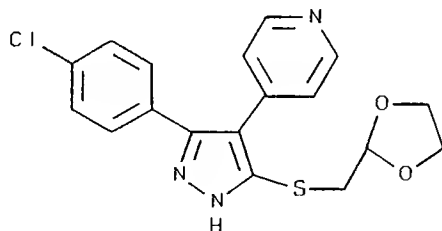


5 To the compound prepared in Example A-453 (264 mg, 0.9 mmol) and *alpha*-methylenebutylolactone (0.08 mL, 0.9 mmol) in ethanol was added a drop of triethylamine. The mixture was stirred overnight. The resulting solid was filtered and triturated with methanol to give the desired

10 product as a pale yellow solid (181 mg, 51% yield). mp 224.2-225.9°C; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub> + approx. 10%TFA) 8.80 (d, 2H); 7.80 (d, 2H); 7.53-7.33 (m, 4H); 4.30-4.05 (m, 2H); 3.50-3.40 (m, 1H); 3.15-2.90 (m, 2H); 2.32-2.20 (m, 1H) 2.10-1.90 (m, 1H); ESHRMS *m/z* 386.0760 (M+H,

15 C<sub>19</sub>H<sub>17</sub>ClN<sub>3</sub>O<sub>2</sub>S requires 386.0730); Anal. Calc'd for: C<sub>19</sub>H<sub>16</sub>ClN<sub>3</sub>O<sub>2</sub>S: C, 59.14 H, 4.18; N, 10.89. Found: C, 58.97; H, 4.21; N, 10.96.

## Example A-473



20 The above compound was prepared similarly to the compound of Example A-456 using 2-bromomethyl-1,3-dioxolane except the mixture was heated at 80°C for two

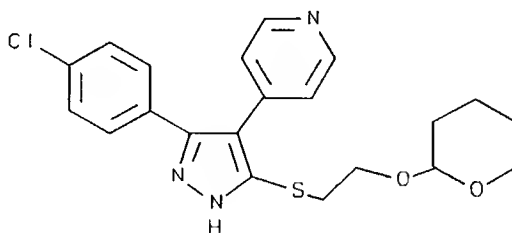
25 hours. The mixture was diluted with water and filtered to give a white solid (502 mg). The solid was recrystallized from ethanol to give the desired product as off-white crystals (280 mg, 43% yield). mp 197.0-

198.2°C;  $^1\text{H}$  NMR (DMSO- $d_6$ ) 13.60 (br s, 1H); 8.60-8.45 (m, 2H); 7.60-7.10 (m, 6H); 5.15-4.85 (m, 1H); 3.95-3.62 (m, 4H); 3.40-2.95 (m, 2H); ESHRMS  $m/z$  374.0741 (M+H,

$\text{C}_{18}\text{H}_{17}\text{ClN}_3\text{O}_2\text{S}$  requires 374.0730); Anal. Calc'd for:

5  $\text{C}_{18}\text{H}_{16}\text{ClN}_3\text{O}_2\text{S}$ : C, 57.83 H, 4.31; N, 11.24. Found: C, 57.69; H, 4.41; N, 11.15.

#### Example A-474



10

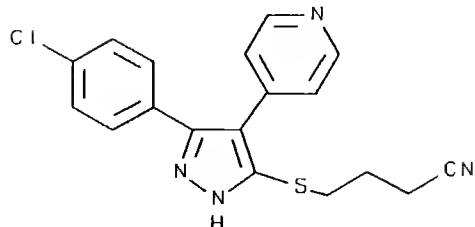
The above compound was prepared similarly to the compound of Example A-456 using 2-(2-bromoethoxy)tetrahydro-2H-pyran except that the mixture was heated at 80 °C for four hours. The mixture was allowed to cool and partitioned between ethyl acetate and water. The ethyl acetate layer was dried over  $\text{MgSO}_4$  and concentrated in vacuo leaving a solid (737 mg). The solid was recrystallized from ethanol to give the desired product as pale yellow crystals (281 mg, 39% yield). mp 163.2-163.5°C;  $^1\text{H}$  NMR (DMSO- $d_6$ ) 13.80-13.70 (m, 1H), 8.60-8.42 (br s, 1H); 7.60-7.10 (m, 6H); 4.60-4.30 (m, 1H); 3.90-2.90 (m, 6H); 1.70-1.20 (m, 6H); ESHRMS  $m/z$  416.1200 (M+H,  $\text{C}_{21}\text{H}_{23}\text{ClN}_3\text{O}_2\text{S}$  requires 416.1198); Anal. Calc'd for:  $\text{C}_{21}\text{H}_{22}\text{ClN}_3\text{O}_2\text{S}$ : C, 60.64 H, 5.33; N, 10.10. Found: C, 60.49; H, 5.71; N, 9.96.

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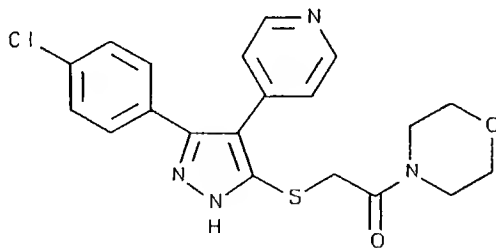
25

## Example A-475



5        The above compound was prepared similarly to the compound of Example A-456 using 4-bromobutyronitrile except the mixture was heated at 55 °C for one hour. The mixture was diluted with water (75 mL) and filtered to give a white solid (567 mg). The solid was  
 10        recrystallized from methanol to give the desired product as white crystals (333 mg, 54% yield). mp 216.7-216.9°C; <sup>1</sup>H NMR (DMSO-d<sub>6</sub> + approx. 10%TFA) 8.80-8.75 (m, 2H); 7.83-7.75 (m, 2H); 7.50-7.35 (m, 4H); 3.10-3.00 (m, 2H); 2.60-2.45 (m, 2H); 1.95-1.80 (m, 2H); ESHRMS m/z  
 15        355.0818 (M+H, C<sub>18</sub>H<sub>16</sub>ClN<sub>4</sub>S requires 355.0784); Anal. Calc'd for: C<sub>18</sub>H<sub>15</sub>ClN<sub>4</sub>S (0.5 H<sub>2</sub>O): C, 59.42 H, 4.43; N, 15.40. Found: C, 59.64; H, 4.11; N, 15.44.

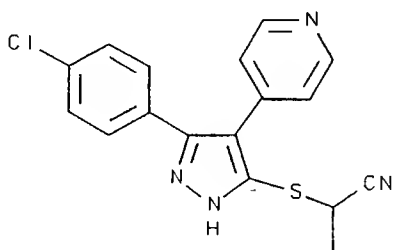
## Example A-476



20        The compound prepared in Example A-461 (416 mg, 1.1 mmol), morpholine (4 mL), O-benzotriazol-1-yl-N,N,N',N'-tetramethyluronium tetrafluoroborate (481 mg, 1.5 mmol) and dimethylformamide (10 mL) were stirred overnight. The mixture was diluted with water (75 mL) and the resulting solid was filtered (363 mg). The solid was recrystallized from ethanol to give the desired product

as a white solid (219 mg, 48% yield). mp 215.4-215.5°C;  
<sup>1</sup>H NMR (DMSO-d<sub>6</sub>) 13.70-13.60 (m, 1H); 8.60-8.50 (m, 2H);  
 7.50-7.10 (m, 6H); 3.93-3.80 (m, 2H); 3.60-3.20 (m, 8H);  
 ESHRMS m/z 415.0995 (M+H, C<sub>20</sub>H<sub>20</sub>ClN<sub>4</sub>O<sub>2</sub>S requires 415.1001);  
 5 Anal. Calc'd for: C<sub>20</sub>H<sub>19</sub>ClN<sub>4</sub>O<sub>2</sub>S: C, 57.90 H, 4.62; N,  
 13.50. Found: C, 57.87; H, 4.86; N, 13.53.

#### Example A-477

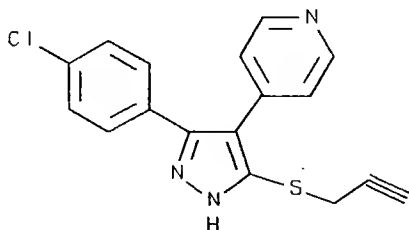


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The above compound was prepared similarly to the  
 compound of Example A-456 using 2-bromopropionitrile  
 except the mixture was heated at 70 °C for one hour. The  
 15 mixture was diluted with water (75 mL) and filtered to  
 give an off-white solid (662 mg). The solid was  
 recrystallized from methanol to give the desired product  
 as a white solid (220 mg, 37% yield). mp 211.1-212.8°C;  
<sup>1</sup>H NMR (DMSO-d<sub>6</sub> + approx. 10%TFA) 8.87-8.80 (m, 2H);  
 20 7.90-7.80 (m, 2H); 7.55-7.45 (m, 6H); 4.42 (q, 1H); 1.50  
 (d, 3H); ESHRMS m/z 341.0628 (M+H, C<sub>18</sub>H<sub>16</sub>ClN<sub>4</sub>S requires  
 341.0628); Anal. Calc'd for: C<sub>17</sub>H<sub>13</sub>ClN<sub>4</sub>S: C, 59.91 H,  
 3.84; N, 16.44. Found: C, 59.64; H, 4.01; N, 16.18.

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#### Example A-478

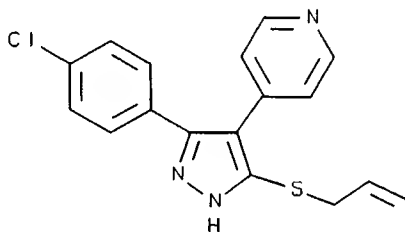


25

The above compound was prepared similarly to the

compound of Example A-456 using propargyl bromide. The mixture was diluted with water (75 mL) and filtered to give a pale yellow solid (577 mg). The solid was triturated with methanol to give the desired product as a white solid (388 mg, 68% yield). mp 212.7-213.2°C; <sup>1</sup>H NMR (DMSO-d<sub>6</sub> + approx. 10%TFA) 8.80 (d, *J* = 6.8 Hz, 2H); 7.82 (d, *J* = 6.8 Hz, 2H); 7.50-7.35 (m, 4H); 3.81 (d, *J* = 2.6 Hz, 2H); 3.05 (t, *J* = 2.6 Hz, 1H); ESHRMS *m/z* 326.0533 (M+H, C<sub>17</sub>H<sub>13</sub>ClN<sub>3</sub>S requires 326.0519); Anal. Calc'd for: C<sub>17</sub>H<sub>12</sub>ClN<sub>3</sub>S (0.2 H<sub>2</sub>O): C, 61.98 H, 3.79; N, 12.76. Found: C, 61.89; H, 3.45; N, 12.67.

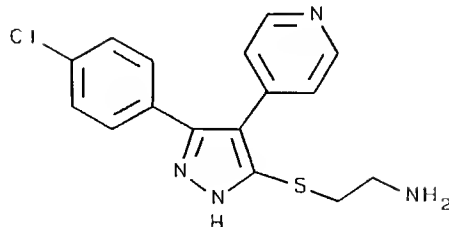
#### Example A-479



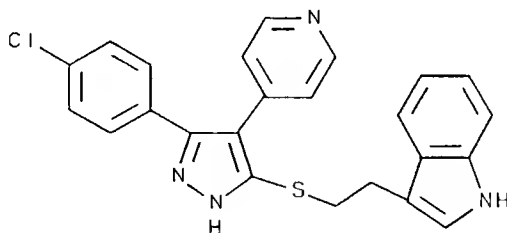
15

The above compound was prepared similarly to the compound of Example A-456 using allyl bromide. The mixture was diluted with water (75 mL) and filtered to give a pale yellow solid (509 mg). The solid was recrystallized from methanol to give the desired product as a pale yellow solid (187 mg, 33% yield). mp 207.3-208.1°C; <sup>1</sup>H NMR (DMSO-d<sub>6</sub> + approx. 10%TFA) 8.80 (d, 2H); 7.80 (d, 2H); 7.50-7.30 (m, 4H); 5.90-5.70 (m, 1H); 5.10-4.95 (m, 2H); 3.62 (d, 2H); ESHRMS *m/z* 328.0693 (M+H, C<sub>17</sub>H<sub>15</sub>ClN<sub>3</sub>S requires 328.0675); Anal. Calc'd for: C<sub>17</sub>H<sub>14</sub>ClN<sub>3</sub>S (0.1 H<sub>2</sub>O): C, 61.94 H, 4.34; N, 12.75. Found: C, 61.83; H, 4.21; N, 12.76.

30

**Example A-480**

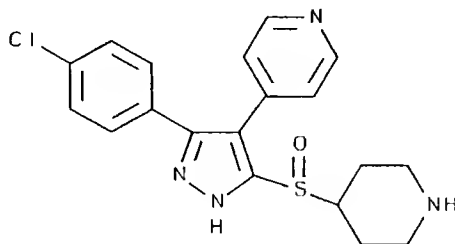
5        The above compound was prepared similarly to the compound of Example A-456 using 2-bromoethylamine except two equivalents of potassium carbonate were used. The mixture was diluted with water (75 mL) and filtered to give a pale yellow solid (509 mg). The solid was  
 10        recrystallized from methanol to give the desired product as a pale yellow solid (262 mg, 45% yield). mp 186.8-187.8°C; <sup>1</sup>H NMR (DMSO-d<sub>6</sub> + approx. 10%TFA) 8.85-8.75 (m, 2H); 8.90 (br s, 2H); 8.85-8.75 (m, 2H); 7.55-7.35 (m, 4H); 3.30-3.00 (m, 4H); ESHRMS m/z 331.0779 (M+H, C<sub>16</sub>H<sub>16</sub>ClN<sub>4</sub>S requires 331.0784); Anal. Calc'd for: C<sub>16</sub>H<sub>15</sub>ClN<sub>4</sub>S (0.5 H<sub>2</sub>O): C, 56.55; H, 4.75; N, 16.49. Found: C, 56.28; H, 4.38; N, 16.20.

**Example A-481**

20        The above compound was prepared similarly to the compound of Example A-456 using 3-(2-bromoethyl)indole.  
 25        The mixture was diluted with water (75 mL) and filtered to give a pale yellow solid (752 mg). The solid was triturated with methanol to give the desired product as a white solid (682 mg, 91% yield). mp 211.9-213.2°C; <sup>1</sup>H NMR (DMSO-d<sub>6</sub> + approx. 10%TFA) 10.80 (s, 1H); 8.72 (d,

2H); 7.71 (d, 2H); 7.55-7.35 (m, 5H); 7.29 (d, 1H); 7.12-6.88 (m, 3H); 3.40-3.30 (m, 2H); 3.05-2.95 (m, 2H); ESHRMS m/z 431.1095 (M+H, C<sub>24</sub>H<sub>20</sub>ClN<sub>4</sub>S requires 431.1097); Anal. Calc'd for: C<sub>24</sub>H<sub>19</sub>ClN<sub>4</sub>S (0.15 H<sub>2</sub>O): C, 66.47 H, 4.49; N, 12.92. Found: C, 66.44; H, 4.51; N, 12.84.

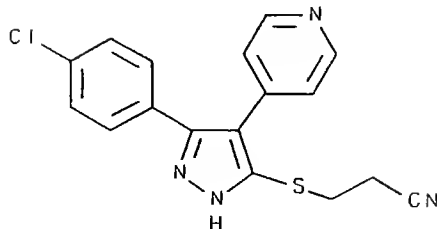
### Example A-482



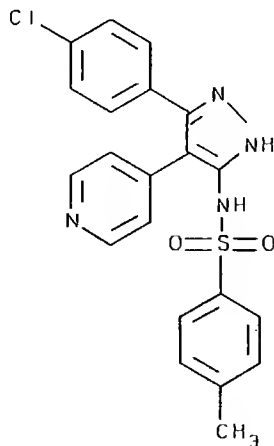
10

The compound of Example A-464 (464 mg, 0.95 mmol) and TFA (8 mL) were mixed in methylene chloride (10 mL) and stirred overnight. The mixture was concentrated in vacuo and the residue was partitioned between ether and water. The aqueous layer was made basic to pH 10 with 2.5N sodium hydroxide and extracted with ethyl acetate (2 x 100 mL). Upon standing overnight, a solid precipitated from the aqueous layer and was filtered to give the desired product as a white solid (183 mg, 50% yield). mp 189.1-190.8°C; <sup>1</sup>H NMR (DMSO-d<sub>6</sub> + approx. 10%TFA) 8.85 (d, 2H); 8.80-8.60 (m 1H); 8.45-8.25 (m, 1H); 7.90 (d, 2H); 7.55-7.30 (m, 4H); 3.65-3.20 (m 3H); 3.10-2.80 (m 2H); 2.20-2.00 (m, 1H); 1.90-1.50 (m, 3H); ESHRMS m/z 387.1032 (M+H, C<sub>19</sub>H<sub>20</sub>ClN<sub>4</sub>OS requires 387.1046); Anal. Calc'd for: C<sub>19</sub>H<sub>20</sub>ClN<sub>4</sub>OS (2 H<sub>2</sub>O): C, 53.96 H, 5.48; N, 13.25. Found: C, 53.75; H, 4.99; N, 13.21.

25

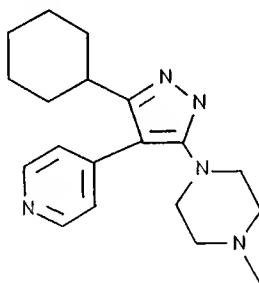
**Example A-483**

5        The above compound was prepared similarly to the compound of Example A-456 using 3-bromopropionitrile. The mixture was diluted with water (75 mL) and extracted into ethyl acetate, which was dried over  $\text{MgSO}_4$  and concentrated in vacuo leaving an orange waxy solid (523  
10 mg). The solid was dissolved in  $\text{CH}_3\text{CN}$  and filtered through a pad of silica gel and eluted with ethyl acetate to give a white solid. The solid was triturated with ethyl acetate and filtered to give the desired product as a white solid (76 mg, 13% yield). mp 205.7-206.5°C;  $^1\text{H}$   
15 NMR ( $\text{DMSO}-d_6$  + approx. 10%TFA) 8.80 (d, 2H); 7.80 (d, 2H); 7.55-7.35 (m, 4H); 3.30-3.20 (m, 2H); 2.90-2.80 (m, 2H); ESHRMS  $m/z$  341.0639 ( $\text{M}+\text{H}$ ,  $\text{C}_{19}\text{H}_{20}\text{ClN}_4\text{OS}$  requires 341.0628); Anal. Calc'd for:  $\text{C}_{17}\text{H}_{13}\text{ClN}_4\text{S}$  ( $0.25 \text{ H}_2\text{O}$ ): C, 59.13 H, 3.94; N, 16.22. Found: C, 59.03; H, 3.93; N,  
20 15.90.

**Example A-484**

453

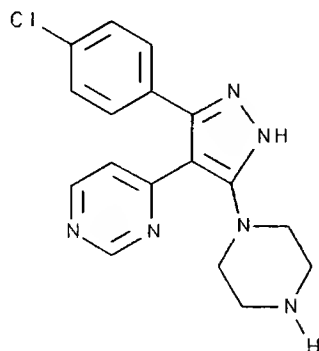
A solution of 5-amino-3-(4-chlorophenyl)-4-(pyridin-4-yl)-pyrazole (200 mg, 0.74 mmol) and toluene sulfonyl chloride (564 mg, 2.94 mmol, prepared as set forth in Example A-427) in pyridine (5 mL) was stirred at 100 °C for two days. The mixture was concentrated *in vacuo* to a brown residue. The residue was chromatographed on a silica gel column eluting with 10% methanol/dichloromethane. The fractions containing the desired product were combined and concentrated to a yellow solid which was washed with diethyl ether and filtered to afford 78 mg (25%) of the desired sulfonamide as a white solid. m.p. 284.3-284.4 °C. <sup>1</sup>H NMR (DMSO/300 MHz) δ 13.33 (brs, 0.8H), 9.94 (brs, 0.75H), 8.48 (brs, 1.75H), 8.22 (brs, 0.3H), 7.63 (d, 1.7H), 7.47 (d, 1.85H), 7.24 (m, 6.45H), 7.02 (brs, 0.25H), 6.81 (brs, 0.20H). ESLRMS m/z 425 (M+H). ESHRMS m/z 425.0848 (M+H, C<sub>21</sub>H<sub>18</sub>N<sub>4</sub>ClS requires 425.0839).

**Example A-485**

1-[cyclohexyl-4-(4-pyridinyl)-1H-pyrazol-3-yl]-4-methylpiperazine.

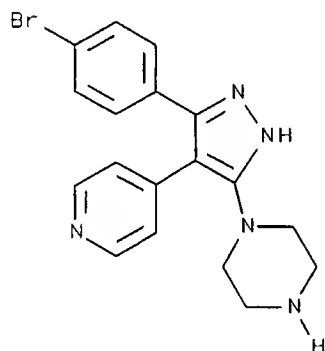
mp >300 °C (decomposed). <sup>1</sup>H NMR (CD<sub>3</sub>OD / 300 MHz) 8.50 (d, 2H, J = 6.0 Hz), 7.51 (d, 2H, J = 5.8 Hz), 2.99-2.93, (m, 4H), 2.52-2.48 (m, 4H), 3.04-3.02 (m, 4H), 2.96 (s, 3H), 2.54-2.49 (m, 1H), 2.31-2.26 (m, 4H), 1.84-1.33 (m, 10H). FABLRMS m/z 326 (M+H).

Additional compounds of the present invention which could be prepared using one or more of the reaction schemes set forth in this application include, but are not limited to, the following:

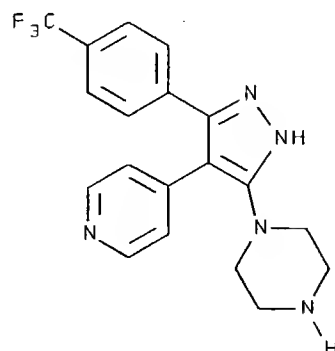


4-[3-(4-chlorophenyl)-5-(1-piperazinyl)-1H-pyrazol-4-yl]pyrimidine ;

5

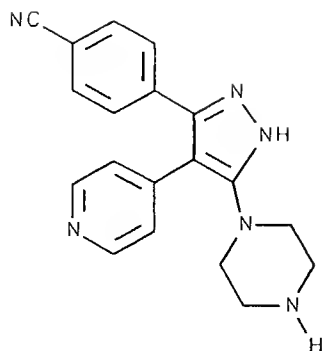


1-[5-(4-bromophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]piperazine ;

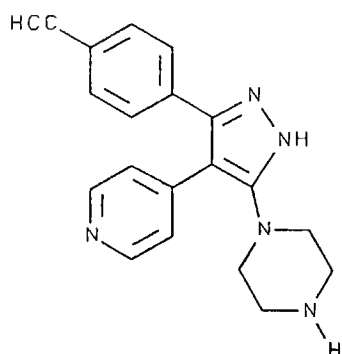


1-[4-(4-pyridinyl)-5-[4-(trifluoromethyl)phenyl]-1H-pyrazol-3-yl]piperazine ;

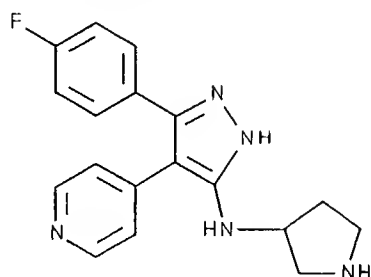
455



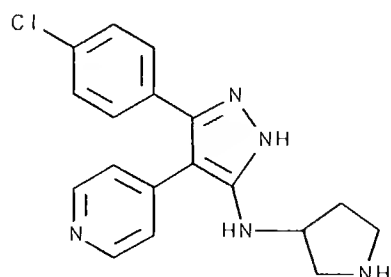
4-[5-(1-piperazinyl)-4-(4-pyridinyl)-  
-1H-pyrazol-3-yl]benzonitrile ;



1-[5-(4-ethynylphenyl)-4-(4-pyridinyl)-  
-1H-pyrazol-3-yl]piperazine ;

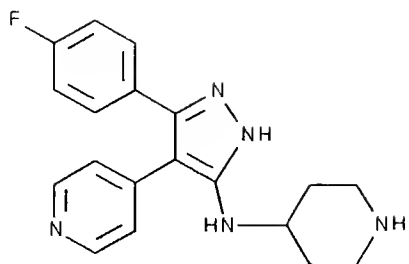


5-(4-fluorophenyl)-4-  
(4-pyridinyl)-N-3-pyrrolidinyl-  
1H-pyrazol-3-amine ;

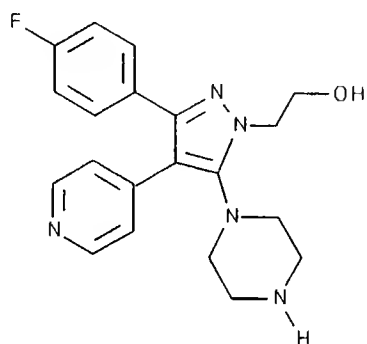


5-(4-chlorophenyl)-4-  
(4-pyridinyl)-N-3-pyrrolidinyl-  
1H-pyrazol-3-amine ;

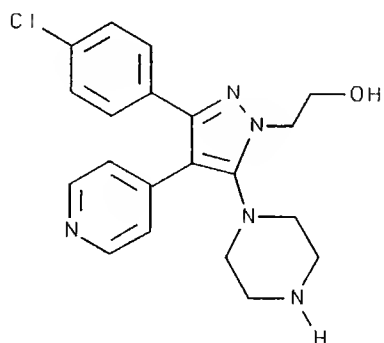
456



N-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-4-piperidinamine ;

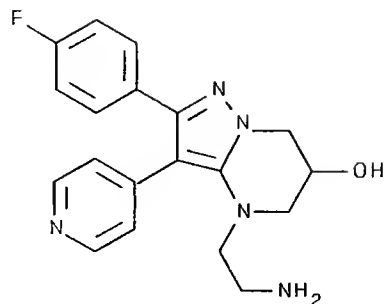


3-(4-fluorophenyl)-5-(1-piperazinyl)-4-(4-pyridinyl)-1H-pyrazole-1-ethanol ;

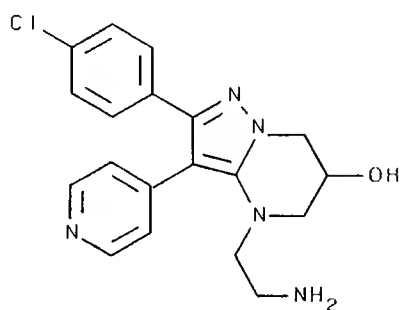


3-(4-chlorophenyl)-5-(1-piperazinyl)-4-(4-pyridinyl)-1H-pyrazole-1-ethanol ;

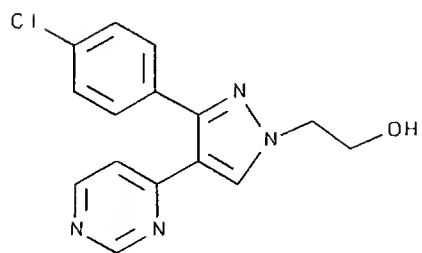
457



4-[2-aminoethyl]-2-(4-fluoro  
phenyl)-4,5,6,7-tetrahydro-  
3-(4-pyridinyl)pyrazolo  
[1,5-a]pyrimidin-6-ol ;

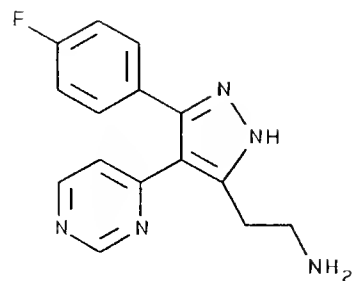


4-[2-aminoethyl]-2-(4-chloro  
phenyl)-4,5,6,7-tetrahydro-  
3-(4-pyridinyl)pyrazolo  
[1,5-a]pyrimidin-6-ol ;

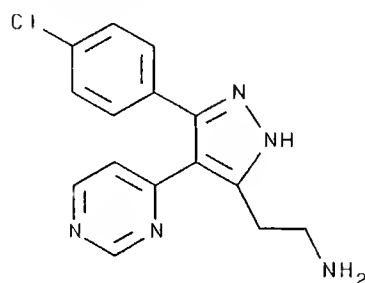


3-(4-chlorophenyl)-4-(4-pyrimidinyl)-  
1H-pyrazole-1-ethanol ;

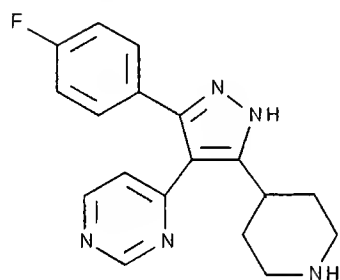
458



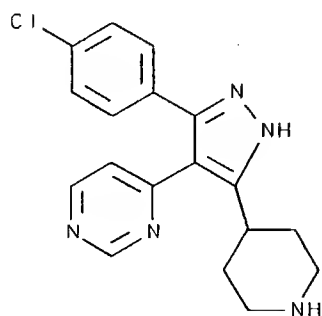
5-(4-fluorophenyl)-4-(4-pyrimidinyl)-  
1H-pyrazole-3-ethanamine ;



5-(4-chlorophenyl)-4-(4-pyrimidinyl)-  
1H-pyrazole-3-ethanamine ;

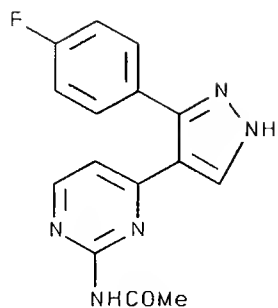


4-[3-(4-fluorophenyl)-5-(4-piperidinyl)-  
1H-pyrazol-4-yl]pyrimidine ;

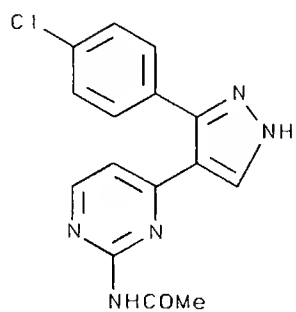


4-[3-(4-chlorophenyl)-5-(4-piperidinyl)-  
1H-pyrazol-4-yl]pyrimidine ;

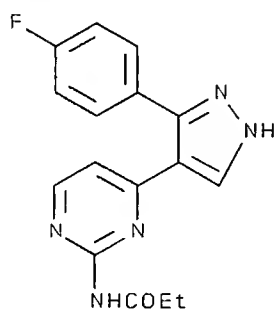
459



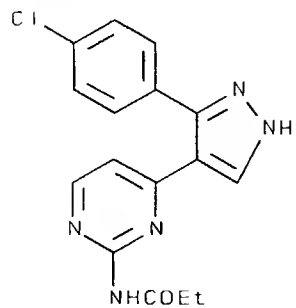
N-[4-[3-(4-fluorophenyl)-1H-pyrazol-4-yl]-2-pyrimidinyl]acetamide ;



N-[4-[3-(4-chlorophenyl)-1H-pyrazol-4-yl]-2-pyrimidinyl]acetamide ;

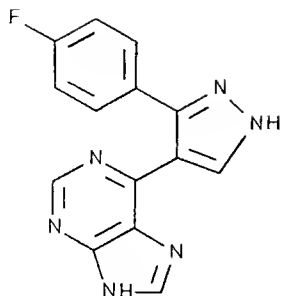


N-[4-[3-(4-fluorophenyl)-1H-pyrazol-4-yl]-2-pyrimidinyl]propanamide ;

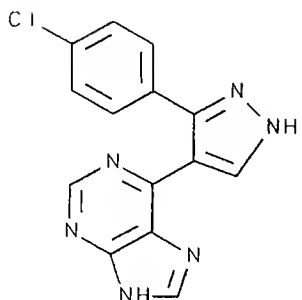


N-[4-[3-(4-fluorophenyl)-1H-pyrazol-4-yl]-2-pyrimidinyl]propanamide ;

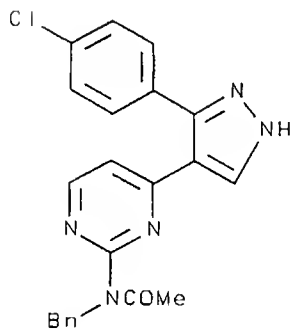
460



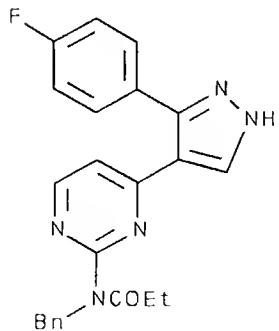
6-[3-(4-fluorophenyl)-1H-pyrazol-4-yl]-1H-purine ;



6-[3-(4-chlorophenyl)-1H-pyrazol-4-yl]-1H-purine ;

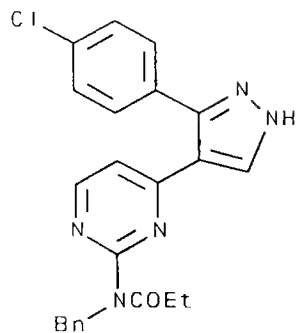


N-[4-[3-(4-chlorophenyl)-1H-pyrazol-4-yl]-2-pyrimidinyl]-N-(benzylmethyl)acetamide ;

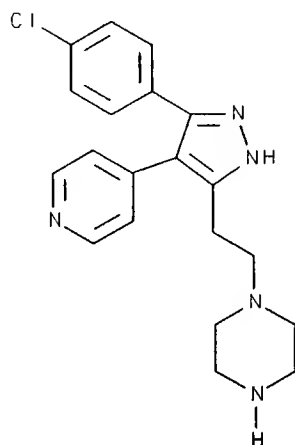


N-[4-[3-(4-fluorophenyl)-1H-pyrazol-4-yl]-2-pyrimidinyl]-N-(benzylmethyl)propanamide ;

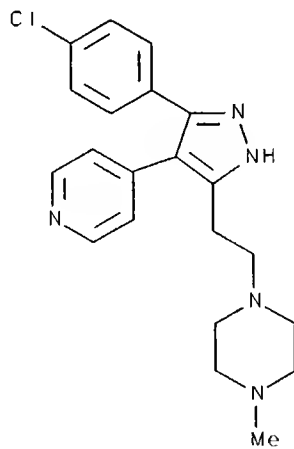
461



N-[4-[3-(4-chlorophenyl)-1H-pyrazol-4-yl]-  
2-pyrimidinyl]-N-(phenylmethyl)propanamide ;



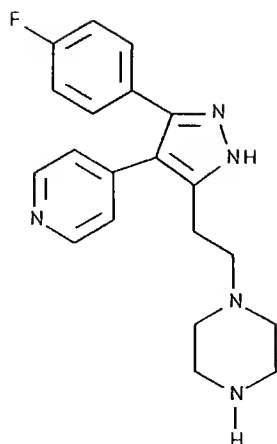
1-[2-[5-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-  
yl]ethyl]piperazine;



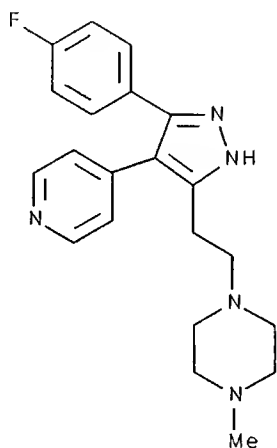
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1-[2-[5-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-  
yl]ethyl]-4-methylpiperazine;

462

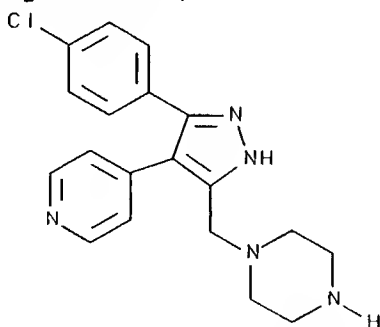


1-[2-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]ethyl]piperazine;



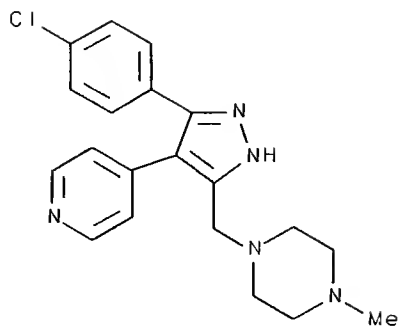
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1-[2-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]ethyl]-4-methylpiperazine;

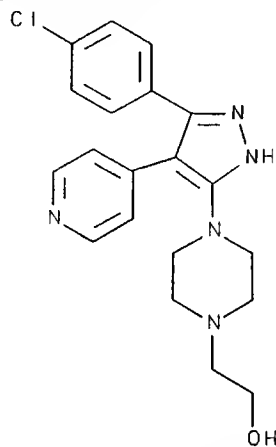


10 1-[[5-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]methyl]piperazine;

463

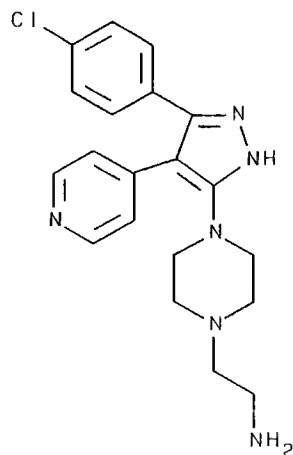


1-[[5-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]methyl]-4-methylpiperazine;



5

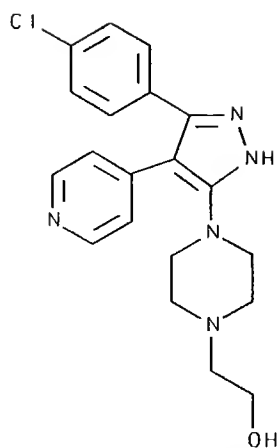
4-[5-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-1-piperazineethanol;



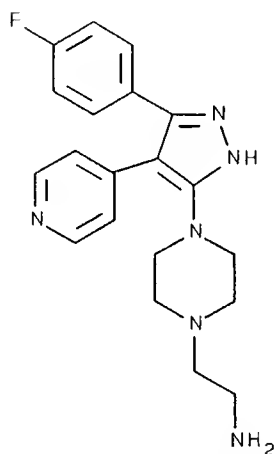
10

4-[5-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-1-piperazineethanamine;

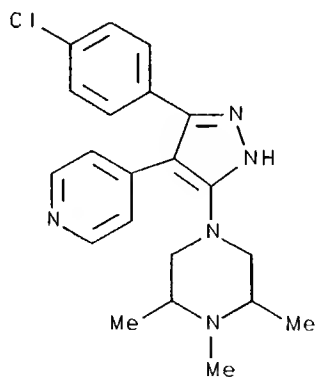
464



4 - [5 - [4 - fluorophenyl) - 4 - (4 - pyridinyl) - 1H - pyrazol - 3 - yl] - 1 - piperazineethanol;

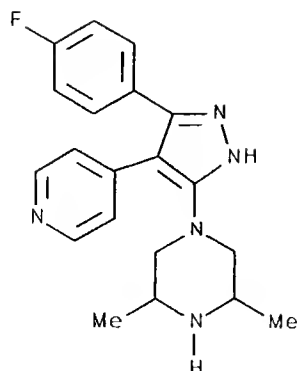


5 4 - [5 - (4 - fluorophenyl) - 4 - (4 - pyridinyl) - 1H - pyrazol - 3 - yl] - 1 - piperazineethanamine;

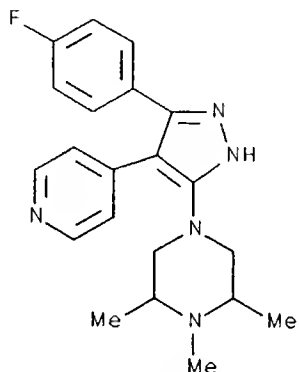


4 - [5 - (4 - chlorophenyl) - 4 - (4 - pyridinyl) - 1H - pyrazol - 3 - yl] - 1,2,6 - trimethylpiperazine;

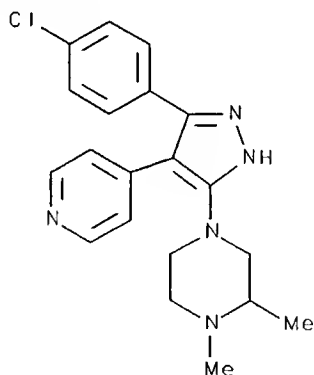
465



1-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-  
3,5-dimethylpiperazine;

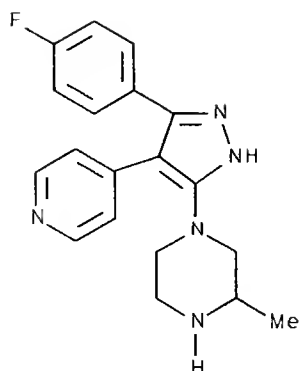


5 4-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-  
1,2,6-trimethylpiperazine;

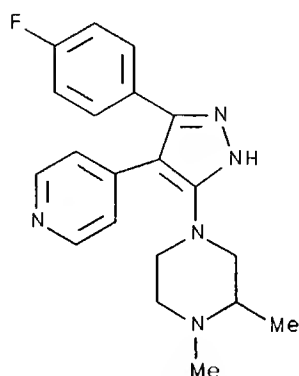


4-[5-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-  
1,2-dimethylpiperazine;

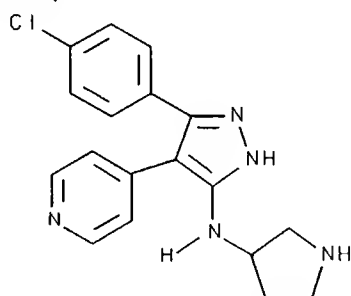
466



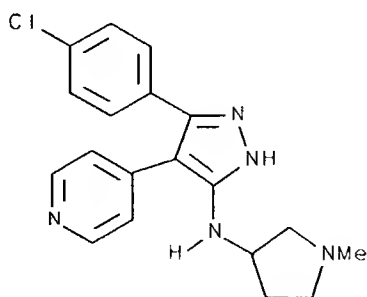
1-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-3-methylpiperazine;



5 4-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-1,2-dimethylpiperazine;



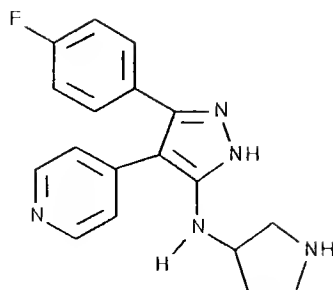
5-(4-chlorophenyl)-4-(4-pyridinyl)-N-3-pyrrolidinyl-1H-pyrazol-3-amine;



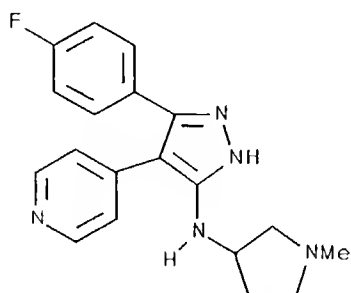
10

5-(4-chlorophenyl)-N-(1-methyl-3-pyrrolidinyl)-4-(4-pyridinyl)-1H-pyrazol-3-amine;

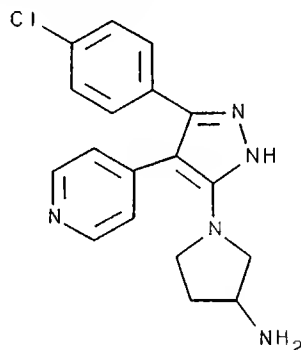
467



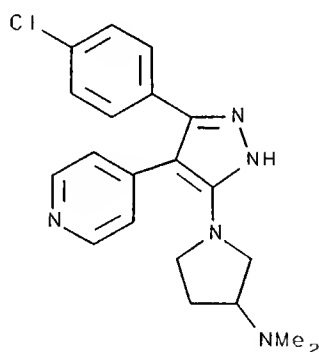
5-(4-fluorophenyl)-4-(4-pyridinyl)-N-3-pyrrolidinyl-1H-pyrazol-3-amine;



5 5-(4-fluorophenyl)-N-(1-methyl-3-pyrrolidinyl)-4-(4-pyridinyl)-1H-pyrazol-3-amine;



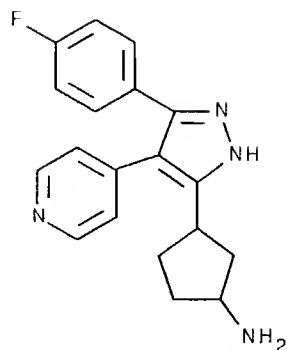
1-[5-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-3-pyrrolidinamine;



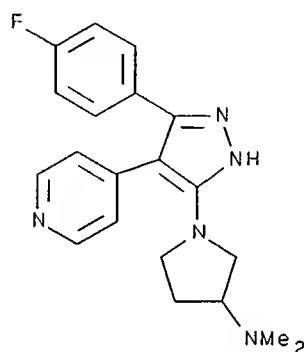
10

1-[5-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-N,N-dimethyl-3-pyrrolidinamine;

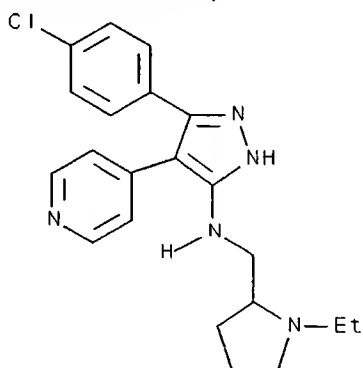
468



1-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-3-pyrrolidinamine;

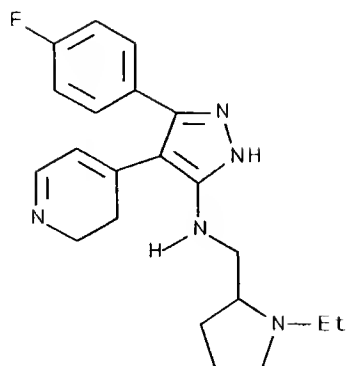


- 5 1-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-N,N-dimethyl-3-pyrrolidinamine;

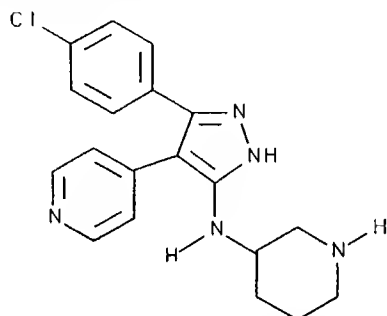


5-(4-chlorophenyl)-N-[(1-ethyl-2-pyrrolidinyl)methyl]-4-(4-pyridinyl)-1H-pyrazol-3-amine;

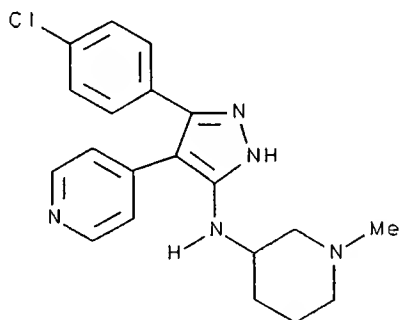
469



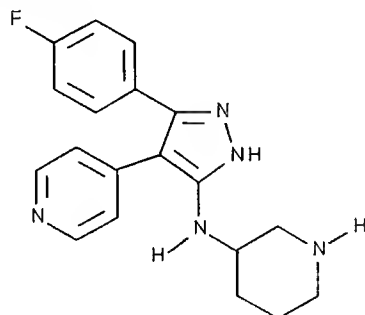
5-(4-fluorophenyl)-N-[(1-ethyl-2-pyrrolidinyl)methyl]-4-(4-pyridinyl)-1H-pyrazol-3-amine;



5 N-[5-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-3-piperidinamine;



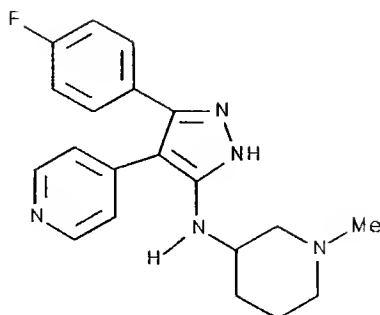
N-[5-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-1-methyl-3-piperidinamine;



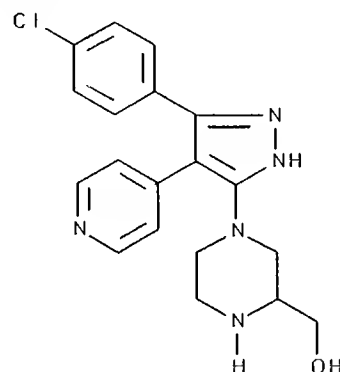
10

N-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-3-piperidinamine;

470

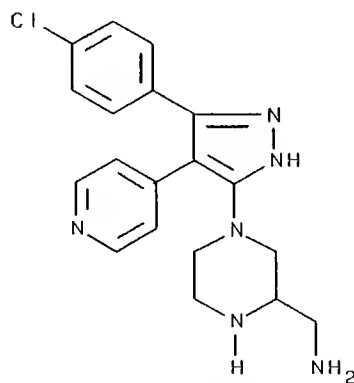


N-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-1-methyl-3-piperidinamine;



5

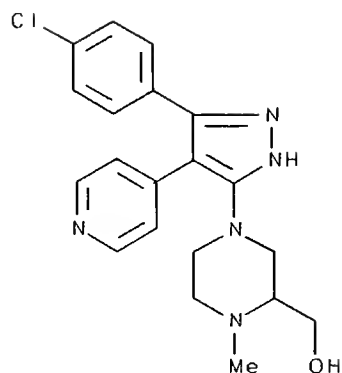
4-[5-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-2-piperazinemethanol;



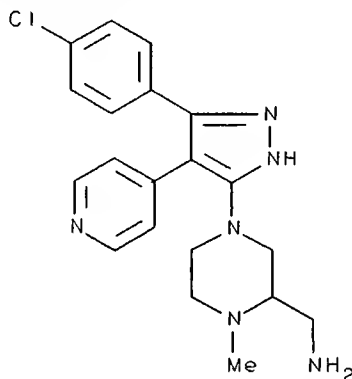
10

4-[5-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-2-piperazinemethanamine;

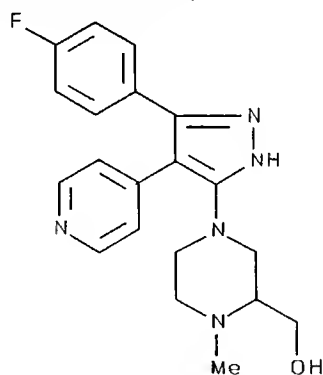
471



4-[5-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-1-methyl-2-piperazinemethanol;

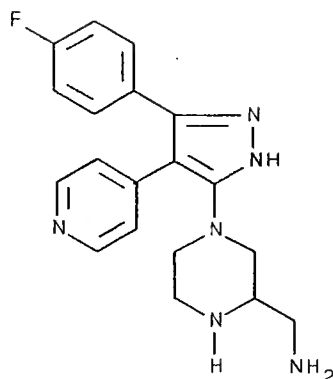


- 5 4-[5-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-1-methyl-2-piperazinemethanamine;

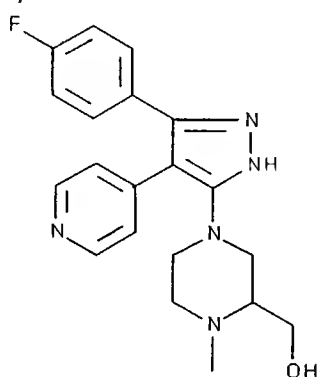


4-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-2-piperazinemethanol;

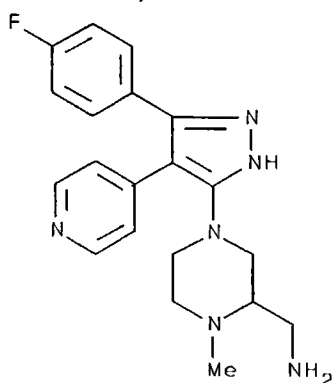
472



4 - [5 - (4-fluorophenyl) - 4 - (4-pyridinyl) - 1H-pyrazol-3-yl] - 2 - piperazinemethanamine;

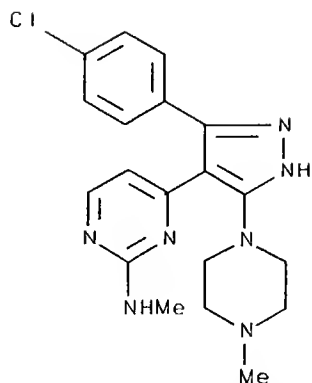


5 4 - [5 - (4-fluorophenyl) - 4 - (4-pyridinyl) - 1H-pyrazol-3-yl] - 1 - methyl-2-piperazinemethanol;

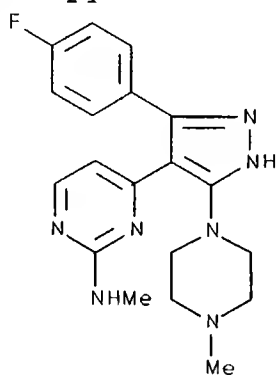


4 - [5 - (4-fluorophenyl) - 4 - (4-pyridinyl) - 1H-pyrazol-3-yl] - 1 - methyl-2-piperazinemethanamine;

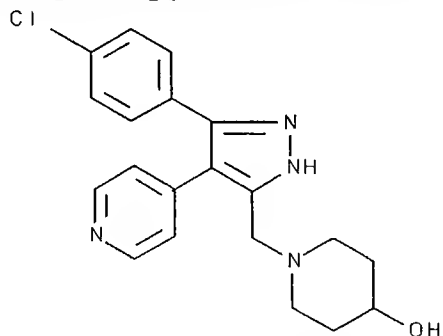
473



4-[3-(4-chlorophenyl)-5-(4-methyl-1-piperazinyl)-1H-pyrazol-4-yl]-N-methyl-2-pyrimidinamine;

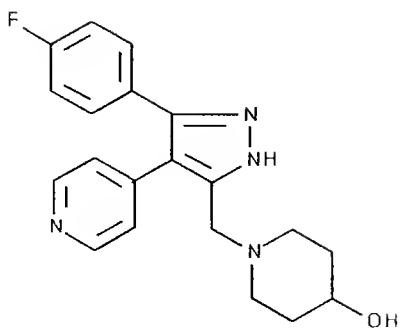


5 4-[3-(4-fluorophenyl)-5-(4-methyl-1-piperazinyl)-1H-pyrazol-4-yl]-N-methyl-2-pyrimidinamine;

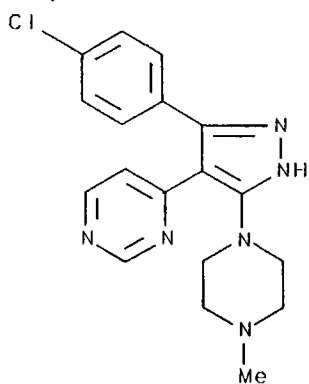


1-[[5-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]methyl]-4-piperidinol;

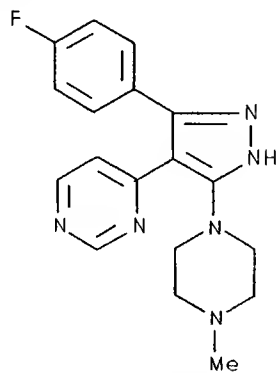
474



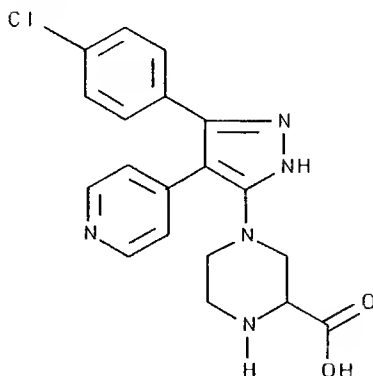
1-[[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]methyl-4-piperidinol;



5 4-[3-(4-chlorophenyl)-5-(4-methyl-1-piperazinyl)-1H-pyrazol-4-yl]pyrimidine;

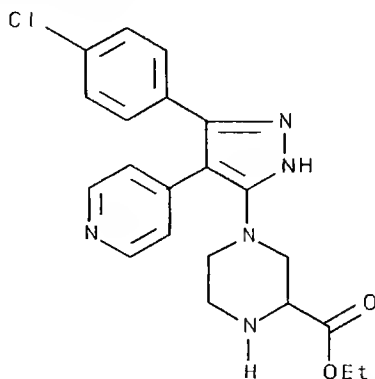


4-[3-(4-fluorophenyl)-5-(4-methyl-1-piperazinyl)-1H-pyrazol-4-yl]pyrimidine;

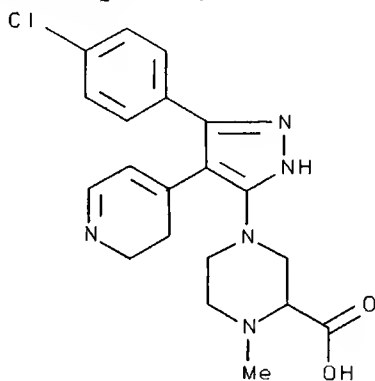


475

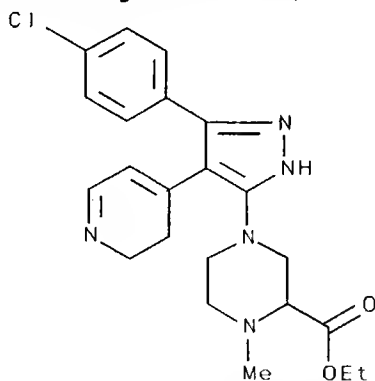
4 - [5 - (4-chlorophenyl) - 4 - (4-pyridinyl) - 1H-pyrazol-3-yl] - 2-piperazinecarboxylic acid;



5 ethyl 4 - [5 - (4-chlorophenyl) - 4 - (4-pyridinyl) - 1H-pyrazol-3-yl] - 2-piperazinecarboxylate;

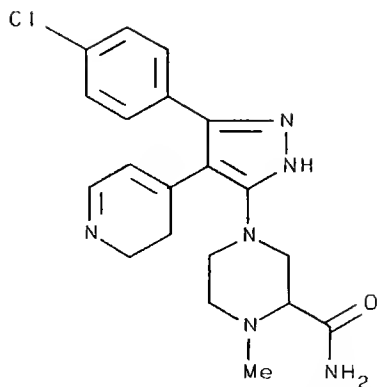


4 - [5 - (4-chlorophenyl) - 4 - (4-pyridinyl) - 1H-pyrazol-3-yl] - 1-methyl-2-piperazinecarboxylic acid;

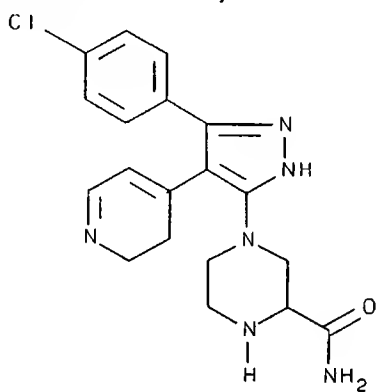


10 ethyl 4 - [5 - (4-chlorophenyl) - 4 - (4-pyridinyl) - 1H-pyrazol-3-yl] - 1-methyl-2-piperazinecarboxylate;

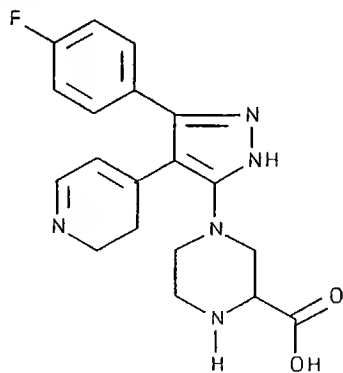
476



4-[5-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-1-methyl-2-piperazinecarboxamide;

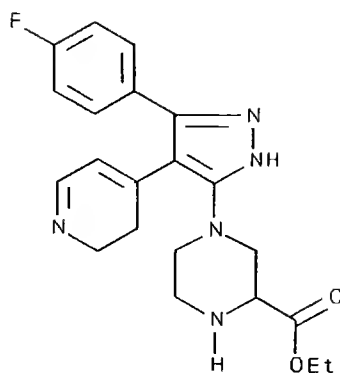


5 4-[5-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-2-piperazinecarboxamide;

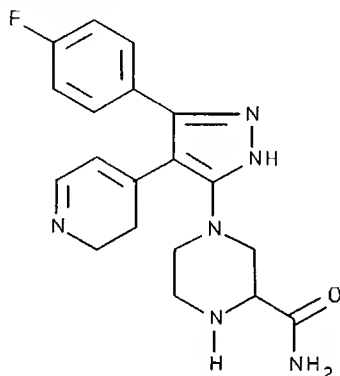


4-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-2-piperazinecarboxylic acid;

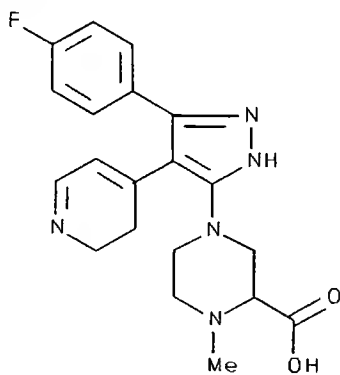
477



ethyl 4-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-2-piperazinecarboxylate;

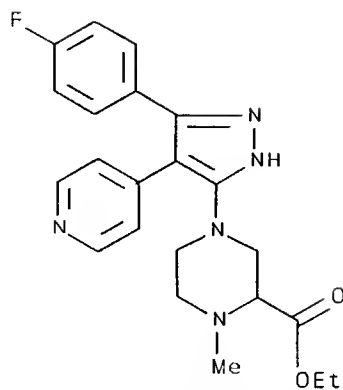


- 5 4-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-2-piperazinecarboxamide;

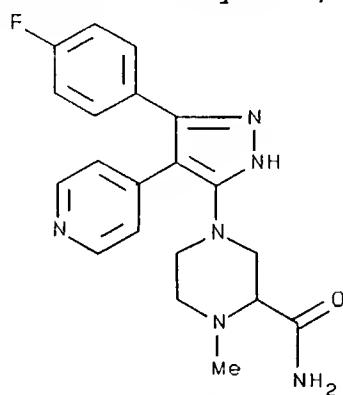


4-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-1-methyl-2-piperazinecarboxylic acid;

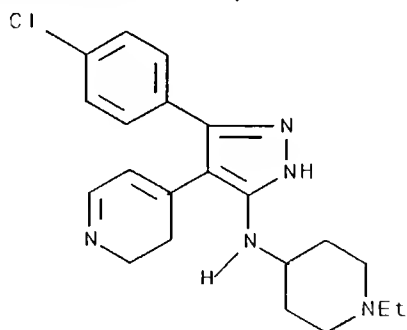
478



ethyl 4-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-1-methyl-2-piperazinecarboxylate;

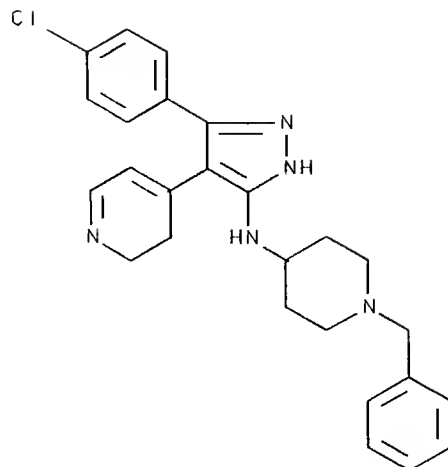


5 4-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-1-methyl-2-piperazinecarboxamide;

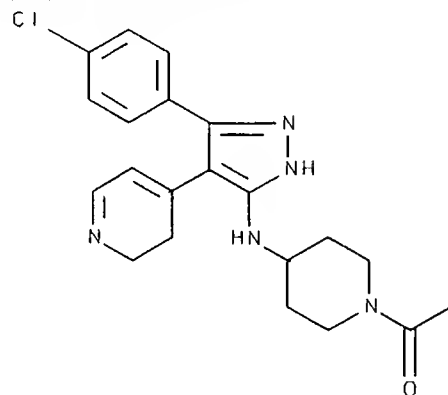


10 N-[5-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-1-ethyl-4-piperidinamine;

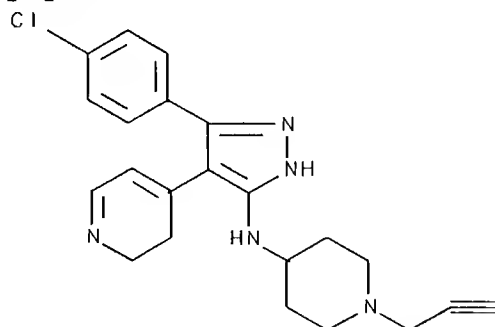
479



N-[5-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-1-(phenylmethyl)-4-piperidinamine;

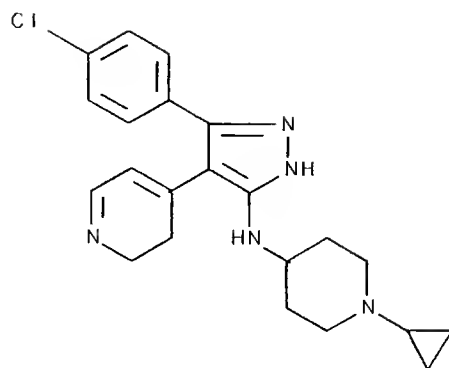


5 1-acetyl-N-[5-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-4-piperidinamine;

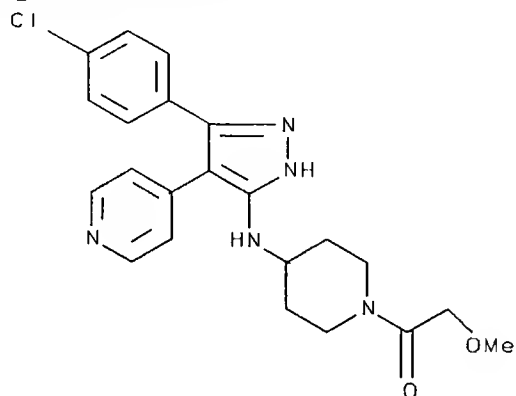


N-[5-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-1-(2-propynyl)-4-piperidinamine;

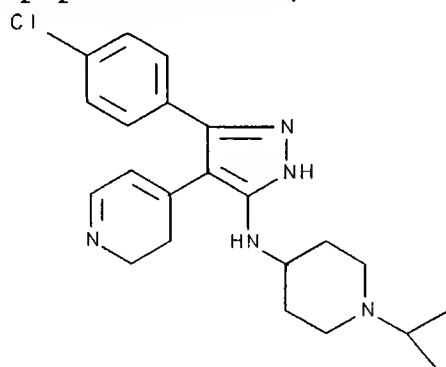
480



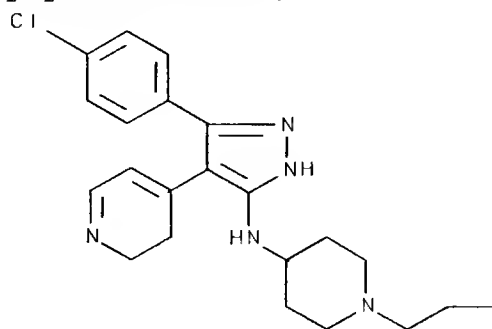
N-[5-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-1-cyclopropyl-4-piperidinamine;



5 N-[5-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-1-(methoxyacetyl)-4-piperidinamine;

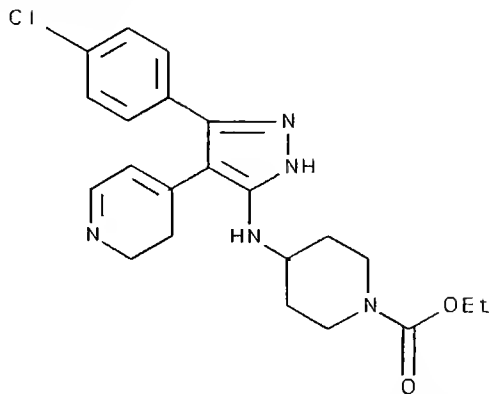


N-[5-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-1-(methylethyl)-4-piperidinamine;

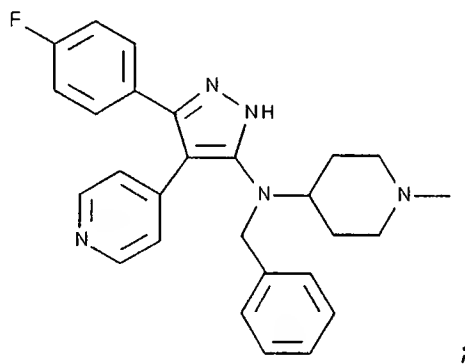
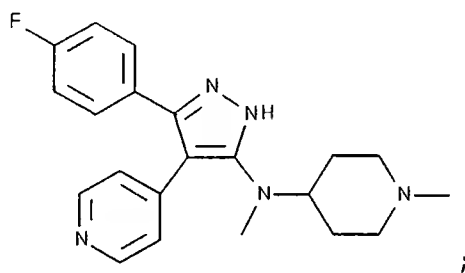


481

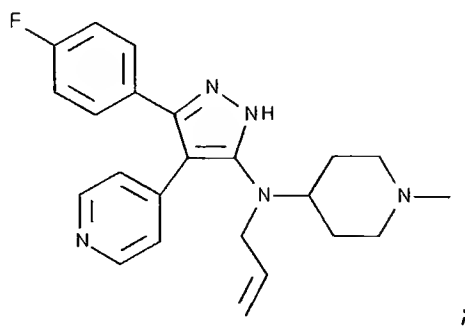
N-[5-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-1-propyl-4-piperidinamine;



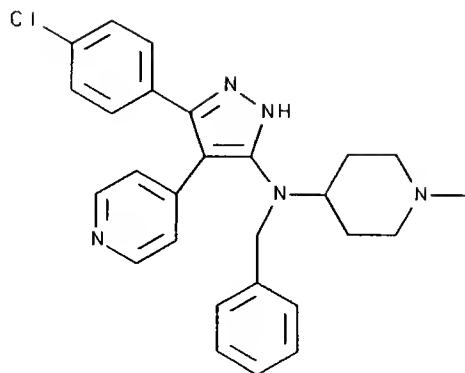
5 ethyl 4-[[5-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]amino]-1-piperidinecarboxylate;



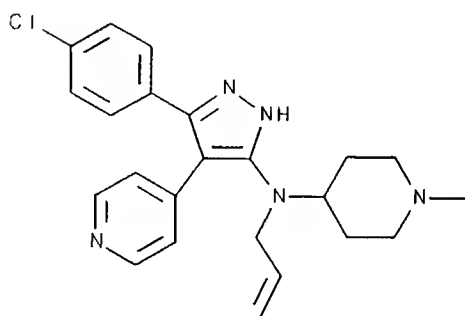
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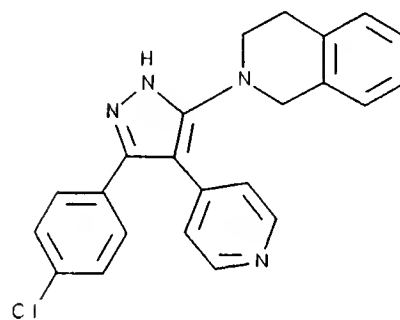
482



;



; and

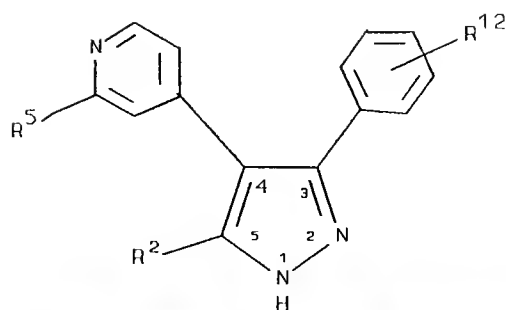


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5

Additional compounds of specific interest include the compounds of Tables 3-3, 3-4, 3-5 and 3-6:

TABLE 3-3



	R <sup>2</sup>	R <sup>5</sup>	R <sup>12</sup>
5	4-piperidinyl	methyl	m- or p-fluoro
	4-piperidinyl	ethyl	m- or p-fluoro
	4-piperidinyl	amino	m- or p-fluoro
	4-piperidinyl	methylamino	m- or p-fluoro
	4-piperidinyl	dimethylamino	m- or p-fluoro
10	4-piperidinyl	ethylamino	m- or p-fluoro
	4-piperidinyl	diethylamino	m- or p-fluoro
	4-piperidinyl	propylamino	m- or p-fluoro
	4-piperidinyl	dipropylamino	m- or p-fluoro
	4-piperidinyl	hydroxyethylamino	m- or p-fluoro
15	4-piperidinyl	1-hydroxy-1,1-dimethylethyl	m- or p-fluoro
	4-piperidinyl	methoxyethylamino	m- or p-fluoro
	4-piperidinyl	methyl	m- or p-chloro
	4-piperidinyl	ethyl	m- or p-chloro
	4-piperidinyl	amino	m- or p-chloro
20	4-piperidinyl	methylamino	m- or p-chloro
	4-piperidinyl	dimethylamino	m- or p-chloro
	4-piperidinyl	ethylamino	m- or p-chloro
	4-piperidinyl	diethylamino	m- or p-chloro
	4-piperidinyl	propylamino	m- or p-chloro
25	4-piperidinyl	dipropylamino	m- or p-chloro
	4-piperidinyl	hydroxyethylamino	m- or p-chloro
	4-piperidinyl	1-hydroxy-1,1-dimethylethyl	m- or p-chloro
	4-piperidinyl	methoxyethylamino	m- or p-chloro
	4-piperidinyl	methyl	m- or p-methyl
30	4-piperidinyl	ethyl	m- or p-methyl
	4-piperidinyl	amino	m- or p-methyl
	4-piperidinyl	methylamino	m- or p-methyl
	4-piperidinyl	dimethylamino	m- or p-methyl

	4-piperidinyl	ethylamino	m- or p-methyl
	4-piperidinyl	diethylamino	m- or p-methyl
	4-piperidinyl	propylamino	m- or p-methyl
	4-piperidinyl	dipropylamino	m- or p-methyl
5	4-piperidinyl	hydroxyethylamino	m- or p-methyl
	4-piperidinyl	1-hydroxy-1,1-dimethylethyl	m- or p-methyl
	4-piperidinyl	methoxyethylamino	m- or p-methyl
	4-piperazinyl	methyl	m- or p-fluoro
	4-piperazinyl	ethyl	m- or p-fluoro
10	4-piperazinyl	amino	m- or p-fluoro
	4-piperazinyl	methylamino	m- or p-fluoro
	4-piperazinyl	dimethylamino	m- or p-fluoro
	4-piperazinyl	ethylamino	m- or p-fluoro
	4-piperazinyl	diethylamino	m- or p-fluoro
15	4-piperazinyl	propylamino	m- or p-fluoro
	4-piperazinyl	dipropylamino	m- or p-fluoro
	4-piperazinyl	hydroxyethylamino	m- or p-fluoro
	4-piperazinyl	1-hydroxy-1,1-dimethylethyl	m- or p-fluoro
	4-piperazinyl	methoxyethylamino	m- or p-fluoro
20	4-piperazinyl	methyl	m- or p-chloro
	4-piperazinyl	ethyl	m- or p-chloro
	4-piperazinyl	amino	m- or p-chloro
	4-piperazinyl	methylamino	m- or p-chloro
	4-piperazinyl	dimethylamino	m- or p-chloro
25	4-piperazinyl	ethylamino	m- or p-chloro
	4-piperazinyl	diethylamino	m- or p-chloro
	4-piperazinyl	propylamino	m- or p-chloro
	4-piperazinyl	dipropylamino	m- or p-chloro
	4-piperazinyl	hydroxyethylamino	m- or p-chloro
30	4-piperazinyl	1-hydroxy-1,1-dimethylethyl	m- or p-chloro
	4-piperazinyl	methoxyethylamino	m- or p-chloro
	4-piperazinyl	methyl	m- or p-methyl
	4-piperazinyl	ethyl	m- or p-methyl
	4-piperazinyl	amino	m- or p-methyl
35	4-piperazinyl	methylamino	m- or p-methyl
	4-piperazinyl	dimethylamino	m- or p-methyl
	4-piperazinyl	ethylamino	m- or p-methyl
	4-piperazinyl	diethylamino	m- or p-methyl
	4-piperazinyl	propylamino	m- or p-methyl
40	4-piperazinyl	dipropylamino	m- or p-methyl

	4-piperazinyl	hydroxyethylamino	m- or p-methyl
	4-piperazinyl	1-hydroxy-1,1-dimethylethyl	m- or p-methyl
	4-piperazinyl	methoxyethylamino	m- or p-methyl
5	aminocyclohexyl	methyl	m- or p-fluoro
	aminocyclohexyl	ethyl	m- or p-fluoro
	aminocyclohexyl	amino	m- or p-fluoro
	aminocyclohexyl	methylamino	m- or p-fluoro
	aminocyclohexyl	dimethylamino	m- or p-fluoro
10	aminocyclohexyl	ethylamino	m- or p-fluoro
	aminocyclohexyl	diethylamino	m- or p-fluoro
	aminocyclohexyl	propylamino	m- or p-fluoro
	aminocyclohexyl	dipropylamino	m- or p-fluoro
	aminocyclohexyl	hydroxyethylamino	m- or p-fluoro
	aminocyclohexyl	1-hydroxy-1,1-dimethylethyl	m- or p-fluoro
15	aminocyclohexyl	methoxyethylamino	m- or p-fluoro
	aminocyclohexyl	methyl	m- or p-chloro
	aminocyclohexyl	ethyl	m- or p-chloro
	aminocyclohexyl	amino	m- or p-chloro
	aminocyclohexyl	methylamino	m- or p-chloro
20	aminocyclohexyl	dimethylamino	m- or p-chloro
	aminocyclohexyl	ethylamino	m- or p-chloro
	aminocyclohexyl	diethylamino	m- or p-chloro
	aminocyclohexyl	propylamino	m- or p-chloro
	aminocyclohexyl	dipropylamino	m- or p-chloro
25	aminocyclohexyl	hydroxyethylamino	m- or p-chloro
	aminocyclohexyl	1-hydroxy-1,1-dimethylethyl	m- or p-chloro
	aminocyclohexyl	methoxyethylamino	m- or p-chloro
	aminocyclohexyl	methyl	m- or p-methyl
	aminocyclohexyl	ethyl	m- or p-methyl
30	aminocyclohexyl	amino	m- or p-methyl
	aminocyclohexyl	methylamino	m- or p-methyl
	aminocyclohexyl	dimethylamino	m- or p-methyl
	aminocyclohexyl	ethylamino	m- or p-methyl
	aminocyclohexyl	diethylamino	m- or p-methyl
35	aminocyclohexyl	propylamino	m- or p-methyl
	aminocyclohexyl	dipropylamino	m- or p-methyl
	aminocyclohexyl	hydroxyethylamino	m- or p-methyl
	aminocyclohexyl	1-hydroxy-1,1-dimethylethyl	m- or p-methyl
	aminocyclohexyl	methoxyethylamino	m- or p-methyl

Still other compounds of specific interest include those compounds of Table 3-3 modified as follows:

(1) The 4-piperidinyl moiety is replaced with a 1-, 2- or 3-piperidinyl moiety; and/or

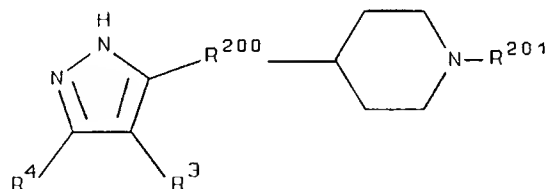
5 (2) The 4-piperidinyl, 3-piperidinyl, 2-piperidinyl or piperazinyl ring is substituted at a nitrogen ring atom with methyl, ethyl, isopropyl, cyclopropyl, propargyl, benzyl, hydroxyethyl, methoxyethyl, or methoxyacetyl; and/or

10 (3) The 1-piperidinyl ring is substituted at a carbon ring atom with methylamino, dimethylamino, ethylamino, diethylamino, isopropylamino, cyclopropylamino, propargylamino, benzylamino, hydroxyethylamino, methoxyethylamino, or  
15 methoxyacetylamino; and/or

(4) The amino group of the aminocyclohexyl is replaced with methylamino, dimethylamino, ethylamino, diethylamino, isopropylamino, methoxyethylamino, or methoxyacetylamino; and/or

20 (5) A linking group selected from the group consisting of methylene, -S-, -O-, and -NH- separates the piperidinyl, piperazinyl or cyclohexyl moiety from the pyrazole nucleus.

TABLE 3-4



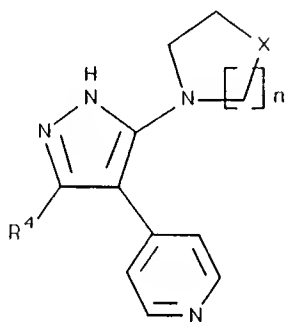
25

	R <sup>4</sup>	R <sup>3</sup>	R <sup>200</sup>	R <sup>201</sup>
	4-pyridyl	4-methylphenyl	H	O
30	4-pyridyl	4-methylphenyl	CH <sub>3</sub>	O
	4-pyrimidyl	4-methylphenyl	H	O
	4-pyrimidyl	4-methylphenyl	CH <sub>3</sub>	O
	4-pyridyl	4-methylphenyl	H	S
	4-pyridyl	4-methylphenyl	CH <sub>3</sub>	S

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	4-pyrimidyl	4-methylphenyl	H	S
	4-pyrimidyl	4-methylphenyl	CH <sub>3</sub>	S
	4-pyridyl	3-methylphenyl	H	O
	4-pyridyl	3-methylphenyl	CH <sub>3</sub>	O
5	4-pyrimidyl	3-methylphenyl	H	O
	4-pyrimidyl	3-methylphenyl	CH <sub>3</sub>	O
	4-pyridyl	3-methylphenyl	H	S
	4-pyridyl	3-methylphenyl	CH <sub>3</sub>	S
	4-pyrimidyl	3-methylphenyl	H	S
10	4-pyrimidyl	3-methylphenyl	CH <sub>3</sub>	S

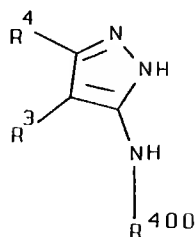
TABLE 3-5



	R <sup>4</sup>	n	X
15	4-chlorophenyl	1	S
	4-chlorophenyl	2	SO
	4-chlorophenyl	2	SO <sub>2</sub>
	4-chlorophenyl	2	CH <sub>2</sub>
	4-chlorophenyl	2	CHCH <sub>3</sub>
20	4-chlorophenyl	2	CHOH
	4-chlorophenyl	1	CH <sub>2</sub>
	4-chlorobenzyl	2	NCH <sub>3</sub>
	2-chlorophenyl	2	NCH <sub>3</sub>
	3,4-methylenedioxyphenyl	2	NCH <sub>3</sub>
25	cyclohexyl	2	NCH <sub>3</sub>
	2-thienyl	2	NCH <sub>3</sub>
	5-chloro-2-thienyl	2	NCH <sub>3</sub>
	4-propynylphenyl	2	NCH <sub>3</sub>
	4-methylsulfoxylphenyl	2	NCH <sub>3</sub>
30	4-methylsulfonylphenyl	2	NCH <sub>3</sub>
	2-(1-methyl-5-chloro)indolyl	2	NCH <sub>3</sub>

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TABLE 3-6



$R^4$	$R^3$	$R^{400}$
p-Cl phenyl	4-pyridyl	$-\text{SO}_2\text{CH}_3$
p-Cl phenyl	4-pyridyl	$-\text{CH}_2\text{CN}$
p-Cl phenyl	4-pyridyl	$-\text{CH}_2-$
p-Cl phenyl		H

5

**BIOLOGICAL EVALUATION****p38 Kinase Assay****Cloning of human p38a:**

The coding region of the human p38a cDNA was obtained by PCR-amplification from RNA isolated from the human monocyte cell line THP.1. First strand cDNA was synthesized from total RNA as follows: 2  $\mu\text{g}$  of RNA was annealed to 100 ng of random hexamer primers in a 10  $\mu\text{l}$  reaction by heating to 70  $^\circ\text{C}$  for 10 minutes followed by 2 minutes on ice. cDNA was then synthesized by adding 1  $\mu\text{l}$  of RNasin (Promega, Madison WI), 2  $\mu\text{l}$  of 50 mM dNTP's, 4  $\mu\text{l}$  of 5X buffer, 2  $\mu\text{l}$  of 100 mM DTT and 1  $\mu\text{l}$  (200 U) of Superscript II <sup>TM</sup> AMV reverse transcriptase. Random primer, dNTP's and Superscript <sup>TM</sup> reagents were all purchased from Life-Technologies, Gaithersburg, MA. The reaction was incubated at 42  $^\circ\text{C}$  for 1 hour. Amplification of p38 cDNA was performed by aliquoting 5  $\mu\text{l}$  of the reverse transcriptase reaction into a 100  $\mu\text{l}$

PCR reaction containing the following: 80  $\mu$ l dH<sub>2</sub>O, 2  $\mu$ l 50 mM dNTP's, 1  $\mu$ l each of forward and reverse primers (50 pmol/ $\mu$ l), 10  $\mu$ l of 10X buffer and 1  $\mu$ l Expand<sup>TM</sup> polymerase (Boehringer Mannheim). The PCR primers incorporated Bam HI sites onto the 5' and 3' end of the amplified fragment, and were purchased from Genosys. The sequences of the forward and reverse primers were 5'-GATCGAGGATTCATGTCTCAGGAGAGGCCCA-3' and 5'-GATCGAGGATTCTCAGGACTCCATCTCTTC-3' respectively. The PCR amplification was carried out in a DNA Thermal Cycler (Perkin Elmer) by repeating 30 cycles of 94 °C for 1 minute, 60 °C for 1 minute and 68 °C for 2 minutes. After amplification, excess primers and unincorporated dNTP's were removed from the amplified fragment with a Wizard<sup>TM</sup> PCR prep (Promega) and digested with Bam HI (New England Biolabs). The Bam HI digested fragment was ligated into BamHI digested pGEX 2T plasmid DNA (PharmaciaBiotech) using T-4 DNA ligase (New England Biolabs) as described by T. Maniatis, *Molecular Cloning: A Laboratory Manual*, 2nd ed. (1989). The ligation reaction was transformed into chemically competent *E. coli* DH10B cells purchased from Life-Technologies following the manufacturer's instructions. Plasmid DNA was isolated from the resulting bacterial colonies using a Promega Wizard<sup>TM</sup> miniprep kit. Plasmids containing the appropriate Bam HI fragment were sequenced in a DNA Thermal Cycler (Perkin Elmer) with Prism<sup>TM</sup> (Applied Biosystems Inc.). cDNA clones were identified that coded for both human p38a isoforms (Lee et al. Nature 372, 739). One of the clones which contained the cDNA for p38a-2 (CSBP-2) inserted in the cloning site of pGEX 2T, 3' of the GST coding region was designated pMON 35802. The sequence obtained for this clone is an exact match of the cDNA clone reported by Lee et al. This expression plasmid allows for the production of a GST-p38a fusion protein.

Expression of human p38a:

GST/p38a fusion protein was expressed from the plasmid pMON 35802 in *E. coli*, strain DH10B (Life Technologies, Gibco-BRL). Overnight cultures were grown in Luria Broth (LB) containing 100 mg/ml ampicillin. The next day, 500 ml of fresh LB was inoculated with 10 ml of overnight culture, and grown in a 2 liter flask at 37 °C with constant shaking until the culture reached an absorbance of 0.8 at 600 nm. Expression of the fusion protein was induced by addition of isopropyl b-D-thiogalactoside (IPTG) to a final concentration of 0.05 mM. The cultures were shaken for three hours at room temperature, and the cells were harvested by centrifugation. The cell pellets were stored frozen until protein purification.

Purification of p38 Kinase- $\alpha$ :

All chemicals were from Sigma Chemical Co. unless noted. Twenty grams of *E. coli* cell pellet collected from five 1 L shake flask fermentations was resuspended in a volume of PBS (140 mM NaCl, 2.7 mM KCl, 10 mM Na<sub>2</sub>HPO<sub>4</sub>, 1.8 mM KH<sub>2</sub>PO<sub>4</sub>, pH 7.3) up to 200 ml. The cell suspension was adjusted to 5 mM DTT with 2 M DTT and then split equally into five 50 ml Falcon conical tubes. The cells were sonicated (Ultrasonics model W375) with a 1 cm probe for 3 X 1 minutes (pulsed) on ice. Lysed cell material was removed by centrifugation (12,000 x g, 15 minutes) and the clarified supernatant applied to glutathione-sepharose resin (Pharmacia).

Glutathione-Sephadex Affinity Chromatography:

Twelve ml of a 50% glutathione sepharose-PBS suspension was added to 200 ml clarified supernatant and incubated batchwise for 30 minutes at room temperature. The resin was collected by centrifugation (600 x g, 5 min) and washed with 2 x 150 ml PBS/1% Triton X-100,

followed by 4 x 40 ml PBS. To cleave the p38 kinase from the GST-p38 fusion protein, the glutathione-sepharose resin was resuspended in 6 ml PBS containing 250 units thrombin protease (Pharmacia, specific activity > 7500 units/mg) and mixed gently for 4 hours at room temperature. The glutathione-sepharose resin was removed by centrifugation (600 x g, 5 min) and washed 2 x 6 ml with PBS. The PBS wash fractions and digest supernatant containing p38 kinase protein were pooled and adjusted to 0.3 mM PMSF.

#### Mono Q Anion Exchange Chromatography:

The thrombin-cleaved p38 kinase was further purified by FPLC-anion exchange chromatography. Thrombin-cleaved sample was diluted 2-fold with Buffer A (25 mM HEPES, pH 7.5, 25 mM beta-glycerophosphate, 2 mM DTT, 5% glycerol) and injected onto a Mono Q HR 10/10 (Pharmacia) anion exchange column equilibrated with Buffer A. The column was eluted with a 160 ml 0.1 M-0.6 M NaCl/Buffer A gradient (2 ml/minute flowrate). The p38 kinase peak eluting at 200 mM NaCl was collected and concentrated to 3-4 ml with a Filtron 10 concentrator (Filtron Corp.).

#### Sephacryl S100 Gel Filtration Chromatography:

The concentrated Mono Q- p38 kinase purified sample was purified by gel filtration chromatography (Pharmacia HiPrep 26/60 Sephacryl S100 column equilibrated with Buffer B (50 mM HEPES, pH 7.5, 50 mM NaCl, 2 mM DTT, 5% glycerol)). Protein was eluted from the column with Buffer B at a 0.5 ml/minute flowrate and protein was detected by absorbance at 280 nm. Fractions containing p38 kinase (detected by SDS-polyacrylamide gel electrophoresis) were pooled and frozen at -80 °C. Typical purified protein yields from 5 L *E. coli* shake flasks fermentations were 35 mg p38 kinase.

### In Vitro Assay

The ability of compounds to inhibit human p38 kinase alpha was evaluated using two in vitro assay methods. In the first method, activated human p38 kinase alpha phosphorylates a biotinylated substrate, PHAS-I (phosphorylated heat and acid stable protein-insulin inducible), in the presence of gamma  $^{32}\text{P}$ -ATP ( $^{32}\text{P}$ -ATP). PHAS-I was biotinylated prior to the assay and provides a means of capturing the substrate which is phosphorylated during the assay. p38 Kinase was activated by MKK6. Compounds were tested in 10 fold serial dilutions over the range of 100  $\mu\text{M}$  to 0.001  $\mu\text{M}$  using 1% DMSO. Each concentration of inhibitor was tested in triplicate.

All reactions were carried out in 96 well polypropylene plates. Each reaction well contained 25 mM HEPES pH 7.5, 10 mM magnesium acetate and 50  $\mu\text{M}$  unlabeled ATP. Activation of p38 was required to achieve sufficient signal in the assay. Biotinylated PHAS-I was used at 1-2  $\mu\text{g}$  per 50  $\mu\text{l}$  reaction volume, with a final concentration of 1.5  $\mu\text{M}$ . Activated human p38 kinase alpha was used at 1  $\mu\text{g}$  per 50  $\mu\text{l}$  reaction volume representing a final concentration of 0.3  $\mu\text{M}$ . Gamma  $^{32}\text{P}$ -ATP was used to follow the phosphorylation of PHAS-I.  $^{32}\text{P}$ -ATP has a specific activity of 3000 Ci/mmol and was used at 1.2  $\mu\text{Ci}$  per 50  $\mu\text{l}$  reaction volume. The reaction proceeded either for one hour or overnight at 30  $^{\circ}\text{C}$ .

Following incubation, 20  $\mu\text{l}$  of reaction mixture was transferred to a high capacity streptavidin coated filter plate (SAM-streptavidin-matrix, Promega) prewetted with phosphate buffered saline. The transferred reaction mix was allowed to contact the streptavidin membrane of the Promega plate for 1-2 minutes. Following capture of biotinylated PHAS-I with  $^{32}\text{P}$  incorporated, each well was washed to remove unincorporated  $^{32}\text{P}$ -ATP three times with 2M NaCl, three washes of 2M NaCl with 1% phosphoric, three washes of distilled water and finally a single wash

of 95% ethanol. Filter plates were air dried and 20  $\mu$ l of scintillant was added. The plates were sealed and counted. Results are shown in Table 4.

A second assay format was also employed that is based on p38 kinase alpha induced phosphorylation of EGFRP (epidermal growth factor receptor peptide, a 21 mer) in the presence of  $^{33}\text{P}$ -ATP. Compounds were tested in 10 fold serial dilutions over the range of 100 $\mu$ M to 0.001 $\mu$ M in 10% DMSO. Each concentration of inhibitor was tested in triplicate. Compounds were evaluated in 50 $\mu$ l reaction volumes in the presence of 25 mM Hepes pH 7.5, 10 mM magnesium acetate, 4% glycerol, 0.4% bovine serum albumin, 0.4mM DTT, 50 $\mu$ M unlabeled ATP, 25  $\mu$ g EGFRP (200 $\mu$ M), and 0.05 uCi gamma  $^{33}\text{P}$ -ATP. Reactions were initiated by addition of 0.09  $\mu$ g of activated, purified human GST-p38 kinase alpha. Activation was carried out using GST-MKK6 (5:1,p38:MKK6) for one hour at 30  $^{\circ}\text{C}$  in the presence of 50 $\mu$ M ATP. Following incubation for 60 minutes at room temperature, the reaction was stopped by addition of 150 $\mu$ l of AG 1X8 resin in 900 mM sodium formate buffer, pH 3.0 (1 volume resin to 2 volumes buffer). The mixture was mixed three times with pipetting and the resin was allowed to settle. A total of 50 $\mu$ l of clarified solution head volume was transferred from the reaction wells to Microlite-2 plates. 150 $\mu$ l of Microscint 40 was then added to each well of the Microlite plate, and the plate was sealed, mixed, and counted.

**TABLE 4**

Example	p38 kinase IC50 ( $\mu$ M)
1	4.6
2	1.5
8	<0.1
16	3.8
23	1.5
25	2.6
26	0.7

	28	0.3
	33	2.5
	34	8.0
	36	12.1
5	38	0.8
	39	1.1
	40	1.3
	42	0.3
	43	<0.1
10	44	<0.1
	45	<0.1
	46	<0.1
	47	3.2
	48	1.8
15	50	2.3
	51	<0.1
	52	0.1
	53	0.9
	54	0.7
20	55	6.4
	143	<0.1

### TNF Cell Assays

#### 25 Method of Isolation of Human Peripheral Blood Mononuclear Cells:

Human whole blood was collected in Vacutainer tubes containing EDTA as an anticoagulant. A blood sample (7 ml) was carefully layered over 5 ml PMN Cell Isolation Medium (Robbins Scientific) in a 15 ml round bottom centrifuge tube. The sample was centrifuged at 450-500 x g for 30-35 minutes in a swing out rotor at room temperature. After centrifugation, the top band of cells were removed and washed 3 times with PBS w/o calcium or magnesium. The cells were centrifuged at 400 x g for 10 minutes at room temperature. The cells were resuspended in Macrophage Serum Free Medium (Gibco BRL) at a concentration of 2 million cells/ml.

#### 40 LPS Stimulation of Human PBMs:

PBM cells (0.1 ml, 2 million/ ml) were co-incubated with 0.1 ml compound (10-0.41  $\mu$ M, final concentration) for 1 hour in flat bottom 96 well microtiter plates.

Compounds were dissolved in DMSO initially and diluted in TCM for a final concentration of 0.1% DMSO. LPS (Calbiochem, 20 ng/ml, final concentration) was then added at a volume of 0.010 ml. Cultures were incubated overnight at 37 °C. Supernatants were then removed and tested by ELISA for TNF- $\alpha$  and IL1- $\beta$ . Viability was analyzed using MTS. After 0.1 ml supernatant was collected, 0.020 ml MTS was added to remaining 0.1 ml cells. The cells were incubated at 37 °C for 2-4 hours, then the O.D. was measured at 490-650 nm.

Maintenance and Differentiation of the U937 Human Histiocytic Lymphoma Cell Line:

U937 cells (ATCC) were propagated in RPMI 1640 containing 10% fetal bovine serum, 100 IU/ml penicillin, 100  $\mu$ g/ml streptomycin, and 2 mM glutamine (Gibco). Fifty million cells in 100 ml media were induced to terminal monocytic differentiation by 24 hour incubation with 20 ng/ml phorbol 12-myristate 13-acetate (Sigma). The cells were washed by centrifugation (200 x g for 5 min) and resuspended in 100 ml fresh medium. After 24-48 hours, the cells were harvested, centrifuged, and resuspended in culture medium at 2 million cells/ml.

LPS Stimulation of TNF production by U937 Cells:

U937 cells (0.1 ml, 2 million/ml) were incubated with 0.1 ml compound (0.004-50  $\mu$ M, final concentration) for 1 hour in 96 well microtiter plates. Compounds were prepared as 10 mM stock solutions in DMSO and diluted in culture medium to yield a final DMSO concentration of 0.1% in the cell assay. LPS (E coli, 100 ng/ml final concentration) was then added at a volume of 0.02 ml. After 4 hour incubation at 37°C, the amount of TNF- $\alpha$  released in the culture medium was quantitated by ELISA. Inhibitory potency is expressed as IC<sub>50</sub> ( $\mu$ M). Results of these TNF Cell Assays are shown in Table 5.

TNF Inhibition: Human Whole Blood Assay

Human peripheral blood is obtained in heparinized tubes. A 190  $\mu$ L aliquot of blood is placed in each well of a 96 well u-bottom plate. A compound or control  
5 vehicle (phosphate buffered saline with dimethylsulfoxide and ethanol) is added to the blood in 10  $\mu$ L aliquots for serial dilutions providing final concentrations of 25, 5, 1 and 0.25  $\mu$ M. The final dimethylsulfoxide and ethanol concentrations are 0.1% and 1.5%, respectively. After  
10 one hour of incubation at 37 °C, 10 mL of lipopolysaccharide (*Salmonella typhosa*, Sigma) in phosphate buffered saline is added resulting in a final concentration of 10 mg/mL. After four to five hours of incubation at 37 °C, the supernatants are harvested and  
15 assayed at 1:10 or 1:20 dilutions for human TNF using ELISA.

TABLE 5

Example	Human PBM Assay IC50 ( $\mu$ M)	U937 Cell Assay IC50 ( $\mu$ M)
5	1	0.5
	2	1.6
	4	0.1
	5	0.274
	7	0.201
10	8	<0.1
	9	0.4
	10	0.7
	12	8.5
	13	4.8
15	14	1.2
	17	1.1
	19	0.3
	20	0.484
	21	1.089
20	22	0.077
	24	3.2
	26	8.2
	27	<0.1
	28	2.7
25	29	0.1
	30	2.2
	31	2.6
	32	0.8
	33	1.053
30	34	2.696
	35	0.4
	36	0.5
	37	0.7
	38	1.4
35	39	1.5
	40	0.2
	41	0.7
	42	0.4
	43	0.7
40	44	<0.1
	45	0.243
	46	0.4
	47	0.477
	48	0.04
45	49	0.329
	50	2.359
	51	0.522
	54	2.2
	55	6.8
	143	0.9
		0.074
		0.13
		0.228
		0.301

### Rat Assay

The efficacy of the novel compounds in blocking the production of TNF also was evaluated using a model based on rats challenged with LPS. Male Harlan Lewis rats [Sprague Dawley Co.] were used in this model. Each rat weighed approximately 300 g and was fasted overnight prior to testing. Compound administration was typically by oral gavage (although intraperitoneal, subcutaneous and intravenous administration were also used in a few instances) 1 to 24 hours prior to the LPS challenge. Rats were administered 30  $\mu$ g/kg LPS [salmonella typhosa, Sigma Co.] intravenously via the tail vein. Blood was collected via heart puncture 1 hour after the LPS challenge. Serum samples were stored at -20 °C until quantitative analysis of TNF- $\alpha$  by Enzyme Linked-Immuno-Sorbent Assay ("ELISA") [Biosource]. Additional details of the assay are set forth in Perretti, M., et al., Br. J. Pharmacol. (1993), 110, 868-874, which is incorporated by reference in this application.

### Mouse Assay

#### Mouse Model Of LPS-Induced TNF Alpha Production:

TNF alpha was induced in 10-12 week old BALB/c female mice by tail vein injection with 100 ng lipopolysaccharide (from S. Typhosa) in 0.2 ml saline. One hour later mice were bled from the retroorbital sinus and TNF concentrations in serum from clotted blood were quantified by ELISA. Typically, peak levels of serum TNF ranged from 2-6 ng/ml one hour after LPS injection.

The compounds tested were administered to fasted mice by oral gavage as a suspension in 0.2 ml of 0.5% methylcellulose and 0.025% Tween 20 in water at 1 hour or 6 hours prior to LPS injection. The 1 hour protocol allowed evaluation of compound potency at Cmax plasma levels whereas the 6 hour protocol allowed estimation of

compound duration of action. Efficacy was determined at each time point as percent inhibition of serum TNF levels relative to LPS injected mice that received vehicle only.

Additional results obtained using the above-  
5 described assays are set forth in Table 6 below. p38  
assay and U937 cell assay results are expressed as  $IC_{50}$   
( $\mu$ m). Mouse-LPS assay results are expressed as percent  
inhibition.

500  
TABLE 6

Example	p38 <sup>1</sup>	p38 <sup>2</sup>	U937	mLPS	mLPS	mLPS
				8h	6h dose	1h, 30mpk
A-212	0.49	0.74	0.0967	20	10	93
A-208	0.104	0.049	0.1896	98	30	97
A-227		0.06				96
A-228	0.76	0.339	0.4173	32	30	92
A-229		1.4	0.4622	76		91
A-230	0.42	0.178				96
A-231		0.174	0.3225	86	30	94
A-232		0.048				96
A-233		0.044				53
A-234		0.103				
A-235		0.104				56
A-236		0.237				94
A-237		0.093	0.087			60
A-238		0.177	0.4016			
A-239		0.034		51	30	87
A-240		0.961		78	30	85
A-241		0.338		79	30	87
A-242		0.047		95	30	87
A-243		0.729				82
A-244		0.099				
A-245		<.001	0.0337			65
A-246	0.403	0.592	0.4952			
A-247		<0.01	0.166			
A-249		0.432		73	30	86
A-250		2.873				
A-251		0.637		32		87
A-252		0.774	1.197	48	30	75
A-253		<.001	0.0044			61
A-254		0.081	0.1411			
A-215		2.34	0.2976	38	30	80
A-256		0.813	0.4562			
A-257	1.081	<.01	0.5167			
A-213		0.22				57
A-258		0.48	1.2083			68
A-259		0.17	0.7574			62
A-210	0.16		0.1983	85	30	93
A-260		0.23	1.2821	47	30	79
A-214		0.06	1.4006			70
A-261		0.008	0.2542	48	30	92
A-216		0.018	1.8287	27	30	91
A-262		<0.1	0.3267			45
A-263	<0.01	<0.1	0.5434			49

Example	p38 <sup>1</sup>	p38 <sup>2</sup>	U937	mLPS	mLPS	mLPS
				8h	6h dose	1h, 30mpk
A-264			0.2594			61
A-265		<0.1	0.6016			32
A-266			0.5393			0
A-267		0.43	2.6681			80
A-268		<0.01	0.0074			11
A-217	0.697		0.3486			9
A-269			>10 uM			51
A-270		0.015	0.3466			53
A-271		0.216	4.2144			68
A-272	0.073		0.583			-8
A-273	6.98		>10			43
A-274	<0.1		0.92	21	30	
A-275	10.14 2		>10			
A-276	0.176		0.45	-24	30	
A-277	0.026			33	30	
A-278	0.285		2.3	62	30	
A-279	0.005		0.7	64	30	
A-280	0.134			15	30	
A-281	0.053			22	30	
A-218	0.044			18	30	
A-282	0.045		0.0973	30	30	
A-283	<0.1		0.7998	-20	30	
A-284	0.98		0.5088	-1		
A-285	<0.1		0.1795	11	30	
A-286	0.057		0.09	29	30	
A-287	0.041		0.27	-24	30	
A-288	0.017		0.3	40	30	
A-289	<0.1		0.14	44	30	
A-290			6.0191	4	30	
A-291	0.388		1.1309	36	30	
A-292	1.15		>10			
A-293	0.73					
A-294	0.015		0.5	61	30	
A-295	7.66		>10	94	30	
A-296	26					
A-297	0.52		0.17	89	30	

<sup>1</sup> p38 $\alpha$  in vitro assay results based on PHAS-I assay procedure

<sup>2</sup> p38 $\alpha$  in vitro assay results based on EGFRP assay procedure

Induction And Assessment Of Collagen-Induced Arthritis In Mice:

Arthritis was induced in mice according to the procedure set forth in J.M. Stuart, Collagen Autoimmune Arthritis, Annual Rev. Immunol. 2:199 (1984), which is incorporated herein by reference. Specifically, arthritis was induced in 8-12 week old DBA/1 male mice by injection of 50  $\mu$ g of chick type II collagen (CII) (provided by Dr. Marie Griffiths, Univ. of Utah, Salt Lake City, UT) in complete Freund's adjuvant (Sigma) on day 0 at the base of the tail. Injection volume was 100  $\mu$ l. Animals were boosted on day 21 with 50  $\mu$ g of CII in incomplete Freund's adjuvant (100  $\mu$ l volume). Animals were evaluated several times each week for signs of arthritis. Any animal with paw redness or swelling was counted as arthritic. Scoring of arthritic paws was conducted in accordance with the procedure set forth in Wooley et al., Genetic Control of Type II Collagen Induced Arthritis in Mice: Factors Influencing Disease Susceptibility and Evidence for Multiple MHC Associated Gene Control., Trans. Proc., 15:180 (1983). Scoring of severity was carried out using a score of 1-3 for each paw (maximal score of 12/mouse). Animals displaying any redness or swelling of digits or the paw were scored as 1. Gross swelling of the whole paw or deformity was scored as 2. Ankylosis of joints was scored as 3. Animals were evaluated for 8 weeks. 8-10 animals per group were used.

Preparation And Administration Of Compounds:

The compounds tested on mice having collagen-induced arthritis were prepared as a suspension in 0.5% methylcellulose (Sigma, St. Louis, MO), 0.025% Tween 20 (Sigma). The compound suspensions were administered by oral gavage in a volume of 0.1 ml b.i.d. Administration began on day 20 post collagen injection and continued

daily until final evaluation on day 56. Scoring of arthritic paws was conducted as set forth above. Assay results are set forth in Table 7.

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**TABLE 7**

<u>Compound</u>	<u>% Inhibition of Arthritis</u>
A-210	58.5 @ 15 mpk
A-172	49.3 @ 100 mpk
A-189	51.6 @ 30 mpk
10 A-208	97.5 @ 60 mpk
A-208	75.0 @ 60 mpk

Additional results for selected compounds obtained using the above-described assays are set forth in Tables 8, 9 and 10 below:

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**TABLE 8**

Example	Rat LPS Assay % Inhibition (Dose in mg/kg)	TNF Inhibition-Human Whole Blood Assay ( $\mu$ M)	p38 $\alpha$ Kinase Assay IC <sub>50</sub> in $\mu$ M (% DMSO)
A-313, Step 1			1.34 (1)
A-313, Step 3	96.0 (20.0)	0.12	0.036 (1) 0.37 (10)
20 A-314, Step 1			0.85 (1) 0.37 (10)
A-314, Step 2	0 (1.0) 53.0 (5.0) 85.0 (20.0)	0.47	0.032 (10)
A-315		1.75	0.049 (10)
A-317	58.0 (3.0) 10.0 (3.0) 69.0 (10.0)	0.45	0.07 (10) 0.11 (10)
25 A-318	54.0 (3.0)	0.167	0.29 (1) 0.58 (10) 0.37 (10) 0.6 (10)
A-319	62.0 (3.0)	>25.0	6.06 (1) 0.13 (10)

	A-320	1.0 (3.0)		0.27 (1) 0.05 (10) 0.15 (10)
	A-321 (dihydrate)		>25.0	0.77 (1)
5	A-321 (monosodium salt dihydrate)	14.0 (3.0)		
	A-322	51.5 (3.0)	4.2	0.15 (10) 0.25 (10)
	A-323	40.0 (30.0) 54.0 (30.0)		0.39 (10)
10	A-324	44.0 (3.0)		0.08 (10)
	A-325	25.0 (3.0) 11.0 (30.0)	0.057	0.021 (1) <0.1 (10)
	A-326	0 (10.0)	>25.0	0.97 (10)
	A-327	83.0 (20.0)	0.18	0.15 (10)
	A-328			0.012 (1)
15	A-331	13.0 (20.0)		>100 (1) 0.64 (10)
	A-332	33.0 (1.0) 26.0 (3.0) 25.0 (5.0) -85.0 (10.0)	0.45	0.04 (1) 0.04 (10) 0.015 (10) <0.1 (10)
	A-333	69.0 (5.0)	0.585	0.052 (10)
	A-334	95.0 (20.0) 57.0 (5.0) 36.0 (1.0)	0.22	0.07 (10)
	A-335		>25.0	89.9 (10)
20	A-336			1.16 (10)
	A-337		>25.0	1.35 (10)
	A-338		0.059	0.018 (10)
	A-339		0.056	0.052 (10)
	A-342	98.0 (20.0)	0.31	0.012 (10)
25	A-343	96.0 (20.0)		0.016 (10)

TABLE 9

Example	Rat LPS Assay % Inhibition (Dose in mg/kg)	TNF Inhibition-Human Whole Blood Assay ( $\mu$ M)	p38 $\alpha$ Kinase Assay IC <sub>50</sub> in $\mu$ M (10% DMSO)
A-350	65 (20)		
A-351	0 (20)	0.49	0.27
A-352	36 (20)	9.8	0.13
A-353	49 (20)	5.3	0.037
A-354	6 (20)	25	0.22
A-355	6 (20)	0.095	0.05
A-356	73 (20)	5.3	<0.01
A-357	74 (20)	0.25	0.12
A-358	71 (20)	1	0.23
A-359	70 (20)	1	0.3
A-360	95 (20) 14 (5) 0 (1)	0.5	0.06
A-361	9 (20)	1	
A-362	6 (20)	5.5	0.69
A-363	6 (20)	25	1.5
A-364	79 (20)	0.255	0.49
A-365	95 (20) 50 (5) 12 (1)	0.057	0.032
A-366	92 (20) DR: 6 (1) 45 (5) 97 (20)	0.29	0.041 0.06 0.04
A-368	88 (20) DR: 28 (1) 41 (5) 97 (20)	0.66	0.042
A-369	94 (20) 52 (5)	0.84	0.019 0.011 0.0027
A-370	90 (20) 46 (5)	1.92	0.16

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A-371	52 (20)	25	7.9
A-372	56 (20)	21	0.53
A-374	88 (20) 0 (5) 3 (1)	0.31	0.38
A-375	43 (20)	28%	2.3
A-376	24 (20)	1	0.032
A-377	84 (20) DR: 32 (1) 67 (5) 96 (20)	0.67	0.004 0.0019
A-378	73 (10)	49%	6.2
A-379	61 (10)	44%	0.19
A-380	85 (30) 62 (10) 33 (3)	32%	0.85
A-385			0.18 1.25
A-386	91 (20)	0.16	0.016
A-387	83 (20)	0.11	0.005
A-388	97 (20) 67 (5)	0.34	0.21

TABLE 10

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Example	Rat LPS Assay % Inhibition (Dose in mg/kg @ 4.0 hours)	TNF Inhibition- Human Whole Blood Assay ( $\mu$ M)	p38 $\alpha$ Kinase Assay IC <sub>50</sub> ( $\mu$ M) (10% DMSO; @ 1.0 hour)
A-389, Step 4	55.0 (5.0) 94.0 (20.0)		0.16
A-389, Step 1			1.72
A-390		>25.0	15.1
A-391	53.0 (20.0)	>25.0	4.83

5	A-392			29.7
	A-393			2.32
	A-394			9.11
	A-395			>100
	A-397			30.0
10	A-398		>25.0	45.6
	A-399			22.9
	A-400		>25.0	4.77
	A-401			21.2
	A-402			28.9
15	A-403		>25.0	4.89
	A-404		>25.0	4.13
	A-405		>25.0	4.85
	A-406		>25.0	7.24
	A-407	21.0 (5.0) 82.0 (20.0)	3.86	0.18
20	A-408	20.0 (5.0) 49.0 (20.0)	11.7	5.59
	A-409	41.0 (5.0) 89.0 (20.0)	5.27	0.21
	A-410	11.0 (5.0) 0 (20.0)		0.21
	A-411	40.0 (5.0) 0 (20.0)		3.37
	A-412	0 (5.0) 0 (20.0)		2.15
25	A-413	45.0 (5.0) 85.0 (20.0)	6.51	0.91
	A-414	3.0 (5.0) 14.0 (20.0)	11.2	9.51
	A-415	17.0 (5.0) 84.0 (84.0)		0.51
	A-416		5.07	0.041
	A-417	40.0 (5.0) 70.0 (20.0)	12.0	0.19
	A-418			0.12

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A-419	24.0 (5.0) 58.0 (10.0)		1.31
A-420	47.0 (5.0) 91.0 (20.0)		0.32
A-427	56.0 (5.0) 77.0 (20.0)	24.1	0.19
A-428		0.68	0.4
A-429			56.3
A-430			>100
A-434			5.84
A-435	10.0 (1.0) 0 (5.0) 14.0 (20.0)	>25.0	0.35
A-436		4.61	2.81
A-437		>25.0	7.76
A-438	49.0 (20.0)	>25.0	0.56
A-439	58.0 (5.0) 93.0 (20.0)	5.63	0.15
A-440			
A-441	14.0 (5.0) 62.0 (20.0)	>25.0	1.21
A-442	51.0 (1.0) 56.0 (5.0) 92.0 (20.0)	0.16	0.022
A-443		4.89	0.47
A-444			6.99
A-445		>25.0	1.08
A-446		3.38	0.9
A-447		>25.0	0.77
A-448	73.0 (5.0) 97.0 (20.0)	0.12	0.084
A-449			59.0
A-450			>100
A-451		15.0	0.078
A-452		0.24	2.87
A-454			8.41

	A-453			10.2
	A-455			12.9
	A-456	36.0 (1.0) 48.0 (5.0) 53.0 (20.0)	0.98	0.12
	A-457		>25.0	0.4
5	A-458		>25.0	8.7
	A-459	0 (1.0) 54.0 (5.0) 80.0 (20.0)	0.26	0.027
	A-459 (salt)		0.28	0.1
	A-460		8.91	1.84
	A-461			30.6
10	A-462		>25.0	1.66
	A-463		>25.0	1.66
	A-464			>100
	A-465			>100
	A-466			20.1
15	A-467			21.4
	A-468	46.0 (1.0) 50.0 (5.0) 94.0 (20.0)		0.3
	A-469	51.0 (5.0) 68.0 (20.0)	7.17	0.095
	A-470			10.4
	A-471			4.92
20	A-472		>25.0	0.39
	A-473	58.0 (20.0)	0.56	0.17
	A-474	59.0 (20.0)	1.47	0.11
	A-475		5.11	0.28
	A-476	35.0 (20.0)	0.97	1.01
25	A-477			0.34
	A-478		0.49	0.18
	A-479		2.97	0.072
	A-480		0.16	0.11

A-481		>25.0	0.2
A-482	15.0 (20.0)	0.69	1.62
A-483		0.51	0.3

5 Also embraced within this invention is a class of  
 pharmaceutical compositions comprising the active  
 compounds of this invention in association with one or  
 more non-toxic, pharmaceutically-acceptable carriers  
 and/or diluents and/or adjuvants (collectively referred  
 10 to herein as "carrier" materials) and, if desired, other  
 active ingredients. The active compounds of the present  
 invention may be administered by any suitable route,  
 preferably in the form of a pharmaceutical composition  
 adapted to such a route, and in a dose effective for the  
 15 treatment intended. The active compounds and composition  
 may, for example, be administered orally, intravascularly  
 (IV), intraperitoneally, subcutaneously, intramuscularly  
 (IM) or topically. For oral administration, the  
 pharmaceutical composition may be in the form of, for  
 20 example, a tablet, hard or soft capsule, lozenges,  
 dispensable powders, suspension or liquid. The  
 pharmaceutical composition is preferably made in the form  
 of a dosage unit containing a particular amount of the  
 active ingredient. Examples of such dosage units are  
 25 tablets or capsules. The active ingredient may also be  
 administered by injection (IV, IM, subcutaneous or jet)  
 as a composition wherein, for example, saline, dextrose,  
 or water may be used as a suitable carrier. The pH of  
 the composition may be adjusted, if necessary, with  
 30 suitable acid, base, or buffer. Suitable bulking,  
 dispersing, wetting or suspending agents, including  
 mannitol and PEG 400, may also be included in the  
 composition. A suitable parenteral composition can also  
 include a compound formulated as a sterile solid  
 35 substance, including lyophilized powder, in injection  
 vials. Aqueous solution can be added to dissolve the

compound prior to injection. The amount of therapeutically active compounds that are administered and the dosage regimen for treating a disease condition with the compounds and/or compositions of this invention  
5 depends on a variety of factors, including the age, weight, sex and medical condition of the subject, the severity of the inflammation or inflammation related disorder, the route and frequency of administration, and the particular compound employed, and thus may vary  
10 widely. The pharmaceutical compositions may contain active ingredients in the range of about 0.1 to 1000 mg, preferably in the range of about 7.0 to 350 mg. A daily dose of about 0.01 to 100 mg/kg body weight, preferably between about 0.1 and about 50 mg/kg body weight and most  
15 preferably between about 0.5 to 30 mg/kg body weight, may be appropriate. The daily dose can be administered in one to four doses per day. In the case of skin conditions, it may be preferable to apply a topical preparation of compounds of this invention to the  
20 affected area two to four times a day. For disorders of the eye or other external tissues, e.g., mouth and skin, the formulations are preferably applied as a topical gel, spray, ointment or cream, or as a suppository, containing the active ingredients in a total amount of, for example,  
25 0.075 to 30% w/w, preferably 0.2 to 20% w/w and most preferably 0.4 to 15% w/w. When formulated in an ointment, the active ingredients may be employed with either paraffinic or a water-miscible ointment base. Alternatively, the active ingredients may be formulated  
30 in a cream with an oil-in-water cream base. If desired, the aqueous phase of the cream base may include, for example at least 30% w/w of a polyhydric alcohol such as propylene glycol, butane-1,3-diol, mannitol, sorbitol, glycerol, polyethylene glycol and mixtures thereof. The  
35 topical formulation may desirably include a compound which enhances absorption or penetration of the active

ingredient through the skin or other affected areas. Examples of such dermal penetration enhancers include dimethylsulfoxide and related analogs. The compounds of this invention can also be administered by a transdermal device. Preferably topical administration will be accomplished using a patch either of the reservoir and porous membrane type or of a solid matrix variety. In either case, the active agent is delivered continuously from the reservoir or microcapsules through a membrane into the active agent permeable adhesive, which is in contact with the skin or mucosa of the recipient. If the active agent is absorbed through the skin, a controlled and predetermined flow of the active agent is administered to the recipient. In the case of microcapsules, the encapsulating agent may also function as the membrane. The transdermal patch may include the compound in a suitable solvent system with an adhesive system, such as an acrylic emulsion, and a polyester patch. The oily phase of the emulsions of this invention may be constituted from known ingredients in a known manner. While the phase may comprise merely an emulsifier, it may comprise a mixture of at least one emulsifier with a fat or an oil or with both a fat and an oil. Preferably, a hydrophilic emulsifier is included together with a lipophilic emulsifier which acts as a stabilizer. It is also preferred to include both an oil and a fat. Together, the emulsifier(s) with or without stabilizer(s) make-up the so-called emulsifying wax, and the wax together with the oil and fat make up the so-called emulsifying ointment base which forms the oily dispersed phase of the cream formulations. Emulsifiers and emulsion stabilizers suitable for use in the formulation of the present invention include Tween 60, Span 80, cetostearyl alcohol, myristyl alcohol, glyceryl monostearate, and sodium lauryl sulfate, among others. The choice of suitable oils or fats for the formulation

is based on achieving the desired cosmetic properties, since the solubility of the active compound in most oils likely to be used in pharmaceutical emulsion formulations is very low. Thus, the cream should preferably be a non-greasy, non-staining and washable product with suitable consistency to avoid leakage from tubes or other containers. Straight or branched chain, mono- or dibasic alkyl esters such as di-isoadipate, isocetyl stearate, propylene glycol diester of coconut fatty acids, isopropyl myristate, decyl oleate, isopropyl palmitate, butyl stearate, 2-ethylhexyl palmitate or a blend of branched chain esters may be used. These may be used alone or in combination depending on the properties required. Alternatively, high melting point lipids such as white soft paraffin and/or liquid paraffin or other mineral oils can be used. Formulations suitable for topical administration to the eye also include eye drops wherein the active ingredients are dissolved or suspended in suitable carrier, especially an aqueous solvent for the active ingredients. The anti-inflammatory active ingredients are preferably present in such formulations in a concentration of 0.5 to 20%, advantageously 0.5 to 10% and particularly about 1.5% w/w. For therapeutic purposes, the active compounds of this combination invention are ordinarily combined with one or more adjuvants appropriate to the indicated route of administration. If administered *per os*, the compounds may be admixed with lactose, sucrose, starch powder, cellulose esters of alkanolic acids, cellulose alkyl esters, talc, stearic acid, magnesium stearate, magnesium oxide, sodium and calcium salts of phosphoric and sulfuric acids, gelatin, acacia gum, sodium alginate, polyvinylpyrrolidone, and/or polyvinyl alcohol, and then tableted or encapsulated for convenient administration. Such capsules or tablets may contain a controlled-release formulation as may be provided in a dispersion of active

compound in hydroxypropylmethyl cellulose. Formulations for parenteral administration may be in the form of aqueous or non-aqueous isotonic sterile injection solutions or suspensions. These solutions and  
5 suspensions may be prepared from sterile powders or granules having one or more of the carriers or diluents mentioned for use in the formulations for oral administration. The compounds may be dissolved in water, polyethylene glycol, propylene glycol, ethanol, corn oil,  
10 cottonseed oil, peanut oil, sesame oil, benzyl alcohol, sodium chloride, and/or various buffers. Other adjuvants and modes of administration are well and widely known in the pharmaceutical art.

All patent documents listed herein are incorporated  
15 by reference.

Although this invention has been described with respect to specific embodiments, the details of these embodiments are not to be construed as limitations.

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515 – 529

MISSING AT THE TIME OF PUBLICATION

Description of parallel array synthesis methodology utilized to prepare compounds of Examples B-i, B-ii, and B-iii.

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Scheme B-1 describes the parallel array reaction blocks that were utilized to prepare compounds of Examples B-0001 through B-1574, and by analogy could also be used to prepare compounds of Examples B-1575 through B-2269.

10 Parallel reactions were performed in multi-chamber reaction blocks. A typical reaction block is capable of performing 48 parallel reactions, wherein a unique compound is optionally prepared in each reaction vessel B1. Each reaction vessel B1 is made of either

15 polypropylene or pyrex glass and contains a frit B2 toward the base of the vessel. Each reaction vessel is connected to the reaction block valve assembly plate B3 via leur-lock attachment or through a threaded connection. Each vessel valve B4 is either opened or

20 closed by controlling the leur-lock position or by the opening or closing of levers B5 within a valve assembly plate row. Optionally, solutions can be either drained or maintained above the vessel frits by leaving the valves in the opened position and controlling the back

25 pressure beneath the valve assembly plate by control of inert gas flow through the inert gas inlet valve B6. The parallel reactions that are performed in these reaction blocks are allowed to progress by incubation in a jacketed, temperature controlled shaking station.

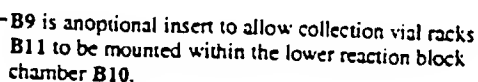
30 Temperature control of the reaction chambers is effected by passing a heat-transfer liquid through jacketed aluminum plates that make contact with the reaction block

mantle B7. Mixing is effected at the shaking station by either vertical orbital shaking of the up-right reaction block or by lateral shaking of the reaction block tilted on its side.

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Functionalized resins are optionally added to each reaction vessel B1 during the course of reaction or at the conclusion of the reaction. These functionalized resins enable the rapid purification of each reaction vessel product. Vacuum filtration of the reaction block apparatus by opening of the vacuum valve B8 allows purified products to be separated from resin-sequestered non-product species. Valve B8 is located on the bottom reaction block chamber B10 which houses the quadrant collection vial racks B11. The desired products are obtained as filtrates in unique collection vials B9. Removal of solvent from these collection vials affords desired products.

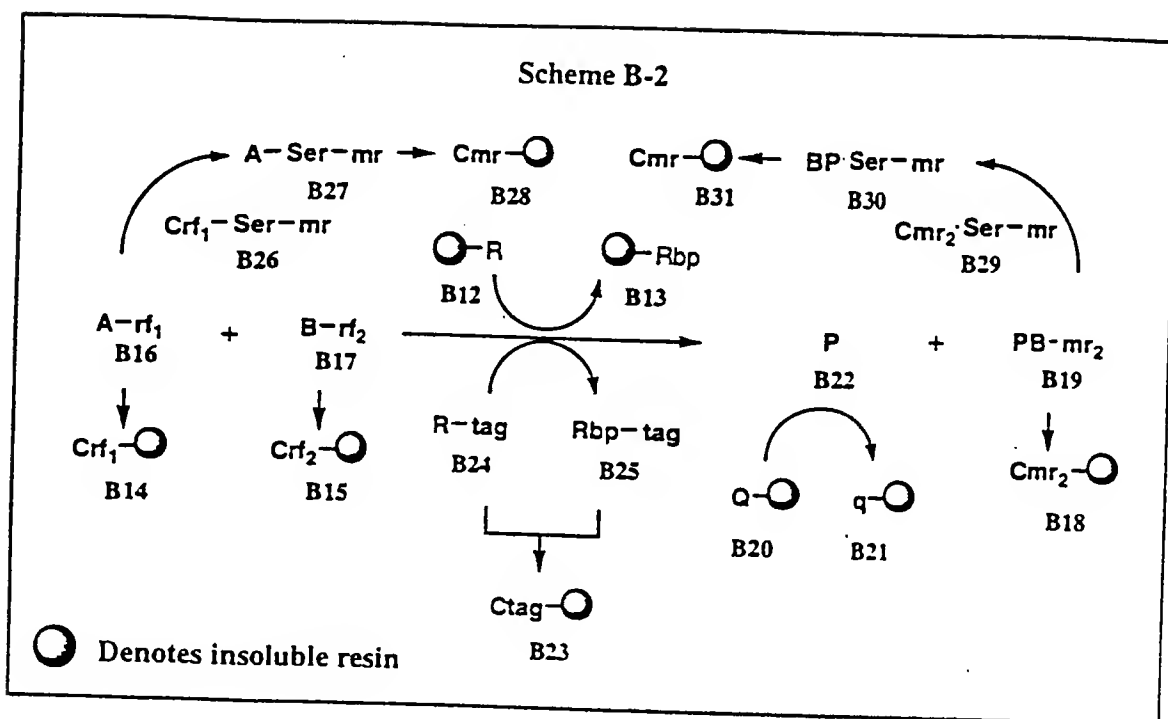
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Scheme B-2 illustrates the various utilizations of functionalized resins to purify reaction vessel products B22 prior to filtration from the fritted vessels B1 into collection vials B9. Said functionalized resins perform as 1) resin-bound reagents B12, which give rise to resin-bound reagent byproducts B13; 2) sequestrants B14 or B15 of excess solution-phase reactants B16 or B17, respectively. Solution-phase reactants B16 and B17 contain inherent reactive functionality  $-rf_1$  and  $-rf_2$

which enable their chemoselective sequestration by the complementary reactive functionality  $-Crf_1$  and  $-Crf_2$  attached to resins B14 and B15; 3) sequestrants B18 of solution-phase byproducts B19. Byproduct B19 contains  
5 molecular recognition functionality  $-mr_2$  which enables its chemoselective sequestration by the complementary functionality  $-Cmr_2$  attached to resin B18; 4) reaction-quenching resins B20 which give rise to quenched resins B21. Resin B20 contains functionality  $-Q$  which mediates  
10 reaction quenching (for instance, proton transfer) of product B22 to form a desired isolable form of product B22. Upon performing reaction quench, the resin B20 is converted to resin B21 wherein  $-q$  represents the spent functionality on resin B21 ; 5) sequestrants B23 of  
15 chemically-tagged reagents B24 and their corresponding reagent byproducts B25. The soluble reagent B24 contains a bifunctional chemical group,  $-tag$ , which is inert to the reaction conditions but is used to enable the post-reaction sequestration of B24 by the complementary  
20 functionality  $-Ctag$  attached to resin B23. Additionally, the soluble reagent byproduct B25, formed during the course of reaction, contains the same chemical function  $-tag$  that also enables its sequestration by resin B23. Additionally, some reactants B16, particularly  
25 sterically-hindered reactants and/or electron deficient nucleophiles, contain poorly sequestrable functionality ( $rf1$  in this case is a poorly sequestable functionality). These poorly sequestable reactants B16 can be transformed *in situ* to more robustly sequestrable species B27 through  
30 their reaction with sequestration-enabling-reagents B26. B26 contain highly reactive, complementary functionality  $Crf_1$  which reacts with B16 to form B27 *in situ*. The

bifunctional molecular recognition functionality,  $mr$ , contained within B26 is also present on the *in situ* derivatized B27. Both B26 and B27 are sequestered by the complementary molecular recognition functionality  
5 attached to resin B28. By analogy, some reactions contain poorly sequesterable byproducts B19, wherein the molecular recognition functionality  $mr_2$  in this case is not able to mediate the direct sequestration of B19 by the complementary functionality attached to resin B18.  
10 Similar use of the bifunctional sequestration-enabling-reagent B29 transforms B19 into the more readily sequesterable species B30. The imparted molecular recognition functionality,  $mr$ , present in B30 is readily sequestered by the complementary functionality,  $Cmr$ ,  
15 attached to resin B31. In some reactions, multiple sequestration resins are utilized simultaneously to perform reaction purifications. Even resins containing incompatible (mutually reactive) functional groups can be used simultaneously because these resins scavenge  
20 complementary functionalized solution phase reactants, reagents, or byproducts from solution phase faster than resin cross-neutralization. Similarly, resins containing mutually reactive or neutralizing reaction-quenching functionality are able to quench solution phase  
25 reactants, products, or byproducts faster than resin cross-neutralization.



Scheme B3 describes the modular robotics laboratory environment that was utilized to prepare compounds of Examples B0001 through Bxxxx. Chemicals that are utilized in the robotics laboratory are weighed and then dissolved or suspended into solvents at Station #1 (Automated Chemistry Prep Station). Thus, solutions or suspensions of known molarity are prepared for use at the other robotics workstations. Station #1 also optionally bar-code labels each chemical solution so that its identity can be read by bar-code scanning at this and other robotics workstations.

Reactions are initiated at the modular Stations #2 and #2 DUP. Station #2DUP is defined as a duplicate of Station #2 and is used to increase capacity within the robotics laboratory. A reaction block is mounted at Station #2 or #2 DUP. Also, racks containing reactants, reagents, solvents, and resin slurries are also mounted at Station #2 or #2 DUP. Under the control of a chemical

informatics mapping file, reactions are initiated by the transfer of reactant solutions, reagent solutions, solvents, and/or resin slurries into each mounted reaction block vessel. The transfer of known volumes of solutions, suspensions, or solvents is mediated by syringes which control a one-up septum piercing/argon purging cannula, a wide-bore resin slurry-despensing cannula, or by a six-up cannula which can simultaneously deliver volumes to a row of six reaction vessels. The reaction block and/or chemical solution racks may be optionally cooled below room temperature during the chemical solution transfer operations. After the transfer of chemical solutions and solvents has been performed by Station#2 or #2DUP, incubation of the reaction block may occur while the reaction block is mounted at the robot station. Preferably, however, the reaction block is removed after all volume transfers are complete and the reaction block is brought to ambient temperature. The reaction block is transferred off-line to either a vertical- or lateral shaking Incubator Station #5.

The Automated weighing/archival Station #3 performs the functions of weighing empty collection vials (to obtain tare weights of collection vials) and also performs the functions of weighing collection vials containing filtered, purified products (to obtain gross weights of collection vials). After product-containing collection vials have been weighed (gross weight determinations) at workstation #3, the collection vial products are optionally redissolved into an organic solvent at workstation #3. Transfer of solvents is accomplished with syringes which control a mounted one-up septum-piercing/argon purging cannula. Each product-containing

collection vial is prepared as a solution of known molarity as directed and recorded by the chemical informatics system. These product solutions may be subsequently mounted at Station #2 or #2DUP for subsequent reaction steps or taken to Station #7 or #7DUP for analytical processing.

Rapid solvent evaporation of product-containing collection vials is accomplished by mounting the collection racks at Savant Automated Solvent Evaporation Stations #4, #4 DUP, or #4 TRIP, wherein #4DUP and #4TRIP are defined as a duplicate and a triplicate of Station #4 to increase the capacity for solvent removal within the robotics laboratory. Commercially available solvent removal stations were purchased from the Savant Company (model # SC210A speedvac unit equipped with model # RVT4104 vapor trap and model # VN100 vapornet cryopump).

Stations #7 and #7DUP perform analytical processing functions. Station #7DUP is defined as a duplicate of Station #7 to increase capacity within the robotics laboratory. Product-containing collection racks are mounted at either of these stations. Each product-containing collection vial is then prepared as a solution of known molarity as directed and recorded by the chemical informatics mapping file. Optionally, this dissolution function is performed by prior processing of the collection vial rack at Station #3 as described above. Station #7 or #7DUP, under the control of the chemical informatics mapping file, transfers aliquots of each product vial into unique and identifiable microtiter plate wells that are utilized to perform analytical determinations.

One such microtiter plate is prepared at Station #7 or #7DUP for subsequent utilization at the Automated HPLC/Mass Spectrometer Station #8 or #8DUP. Station #8DUP is a duplicate of Station #8 to increase the analytical capacity of the robotics laboratory. Stations #8 and #8DUP are commercially available benchtop LC/Mass spec units purchased from Hewlett Packard (model HP1100 HPLC connected to HP1100 MSD (G1946A) mass spectrometer; this unit is also equipped with a model# G1322A solvent degasser, model # G1312A binary pump, a model # G1316A column heater, and a model # G1315A diode array detector. The HP unit has been interfaced with a commercially available autosampler rack (Gilson Company # 215 autosampler). Station #8 or #8DUP is utilized for the determination of product purity and identity by performing high performance liquid chromatography (HPLC) and companion atmospheric pressure chemi-ionization (APCI) or electrospray mass spectrometry for molecular weight determination.

Another microtiter plate is prepared at Station #7 or #7DUP for subsequent utilization at a commercially available flow-probe Varian NMR spectrometer Station #10 (Varian Instruments flow probe NMR, 300 MHz, interfaced with a commercially available Gilson 215 autosampler). Proton, <sup>13</sup>-Carbon, and/or <sup>19</sup>-Fluorine NMR spectra are determined at this Station #10.

Other microtiter plates are optionally mounted at Station #7 or #7DUP for the purpose of preparing product-containing plates for biological assays. Aliquots of product-containing collection vials are transferred to these biological assay microtiter plates under the control of the chemical informatics mapping file. Identity and amount of each transferred product is

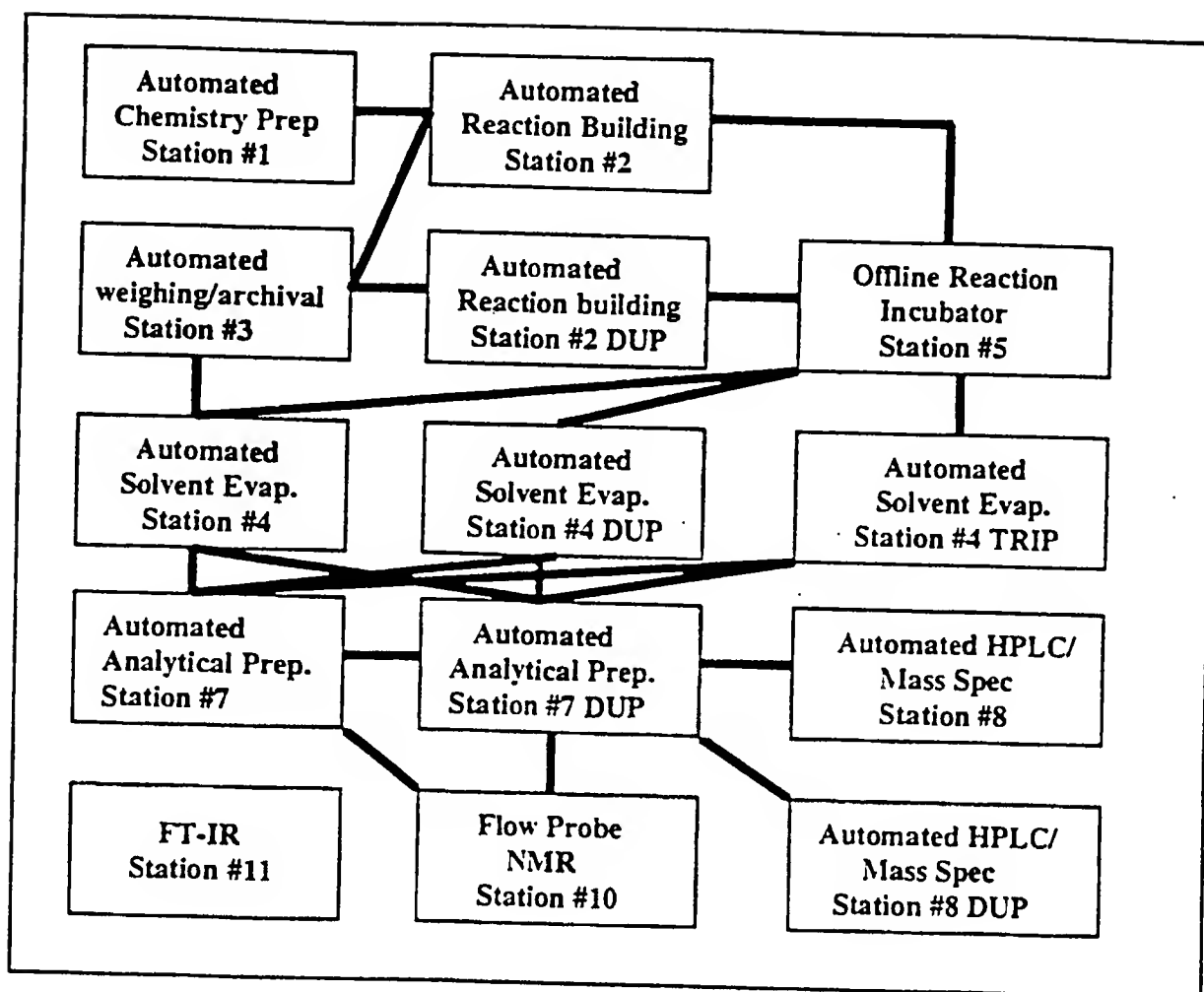
recorded by the chemical informatics system for retrieval by biologists who perform the biological assaying of products.

- 5 The Fourier Transform InfraRed (FT-IR) Spectrometer Station #11 is utilized to analyze resins for the identity of organic functional groups chemically attached to these resins. The resins, as mentioned above, contain chemical functionality utilized as reagents, chemoselective sequestrants, or reaction quenching media for the workup and purification of the crude product mixtures contained within reaction block vessels. The robotics laboratory utilizes a commercially available FT-IR spectrometer purchased from Nicolet Instruments (model # MagnaIR 560 interfaced with an InspectIR microscope for resin mounting and positioning).

#### Scheme B-3

- The lines interconnecting the modular Stations denote the transfer of chemical racks, reaction blocks, and/or collection vial racks from one modular Station to another.

540



The ChemLib IT system is a composite of software running on the client's desktop and software running on a remote server.

The ChemLib IT system is a client/server software application developed to support and document the data handling flow in the robotics laboratory described above. This IT system integrates the chemist with the robotics synthesis laboratory and manages the data generated by this processes.

The software running on the server warehouses all the electronic data for the robotics chemistry unit. This

541

server, a Silicon Graphics IRIX station v6.2, runs the database software, Oracle 7 v7.3.3.5.0, that warehouses the data. Connection from the client's desktop to the server is provided by Oracle's TCP/IP Adapter v2.2.2.1.0 and SQL\*Net v2.2.2.1.0A. SQL\*Net is Oracle's network interface that allows applications running on the client's desktop to access data in Oracles' database. The client's desktop is Microsoft Windows 95. The ChemLib IT system client software is composed of Omnis7 v3.5 and Microsoft Visual C++ v5.0. This composition on the client side is what is herein referred to as ChemLib. ChemLib communicates with the server for its data via Oracle's PL/SQL v2.3.3.4.0. These PL/SQL calls within ChemLib creates a network socket connection to Oracle's SQL\*Net driver and the TCP/IP Adapter thereby allowing access to the data on the server.

A "library" is defined as a composite number of wells, where each well defines a single compound. ChemLib defines a library in a module called the *Electronic Spreadsheet*. The *Electronic Spreadsheet* is then a composite of n-number of wells containing the components that are required to synthesize the compound that exist in each these well(s).

The chemist begins by populating the *Electronic Spreadsheet* with those components required for the compound synthesis. The identity and the availability of these components are defined in the *Building Block Catalog* module of ChemLib. The *Building Block Catalog* is a catalog of a listing of all reagents, solvents, peripherals available in the robotics laboratory. Upon selecting the components for each compound we also

declare the quantity of each component to be utilized. The quantity of each component can be identified by its molarity and volumetric amounts (ul) or by it's solid state form (mg). Therefore a well in the *Electronic Spreadsheet* defines a compound that is identified by its components and the quantity of each of these components.

The assembly or the synthesis of these components for each compound in the *Electronic Spreadsheet* is defined in the *WS Sequence* module of ChemLib. The *Define WS Sequence* module identifies the synthesis steps to be performed at the robotics workstations and any activities to be performed manually or off-line from the robotics workstation. With this module we identify which components from the *Electronic Spreadsheet* and the activity that should be performed with this component in the robotics laboratory. In the *Define WS Sequence* module the chemist chooses from a list of activities to be performed in the robotics laboratory and assembles them in the order in which they are to occur. The ChemLib system takes these set of activities identified, and with the component data in the *Electronic Spreadsheet* assembles and reformats these instructions into terminology for the robotics workstation use. This robotics terminology is stored in a 'sequence' file on a common server that is accessible by the robotics workstation.

The robotics workstation performs the synthesis in a reaction block apparatus as described. Each well in the *Electronic Spreadsheet* is tracked and mapped to a unique location in the reaction block apparatus on the robotics workstation. The compound or product synthesized at the

robotics workstation in the reaction block is then captured into collection vials.

5 The collection vials are first tarred then grossed on the robotics workstation after collecting their products from the reaction block. These weights (tare and gross) are recorded into the ChemLib system with the *Tare/Gross Session* module. The *Tare/Gross Session* module then calculates the product or compound yields and its final  
10 mass.

Preparation of the compound for analytical analysis and screening is defined by the *Analytical WS Setup* module in ChemLib. The *Analytical WS Setup* module identifies the  
15 dilution factor for each well in the *Electronic Spreadsheet*, based on the compound's product yield and the desired molar concentration. This identifies the quantity, in uL, to be transferred at the robotics workstation, to a specific location on the MTP  
20 (microtiter plate) to be sent for analysis and/or biological assaying. The mass spectrometric and HPLC results for each well are recorded and scored into the ChemLib system.

25 The *Dilute/Archive WS* module further identifies each compound by mapping the compound's well from the *Electronic Spreadsheet* to a specific MX block location for long term storage and archival as part of the registration process.

30

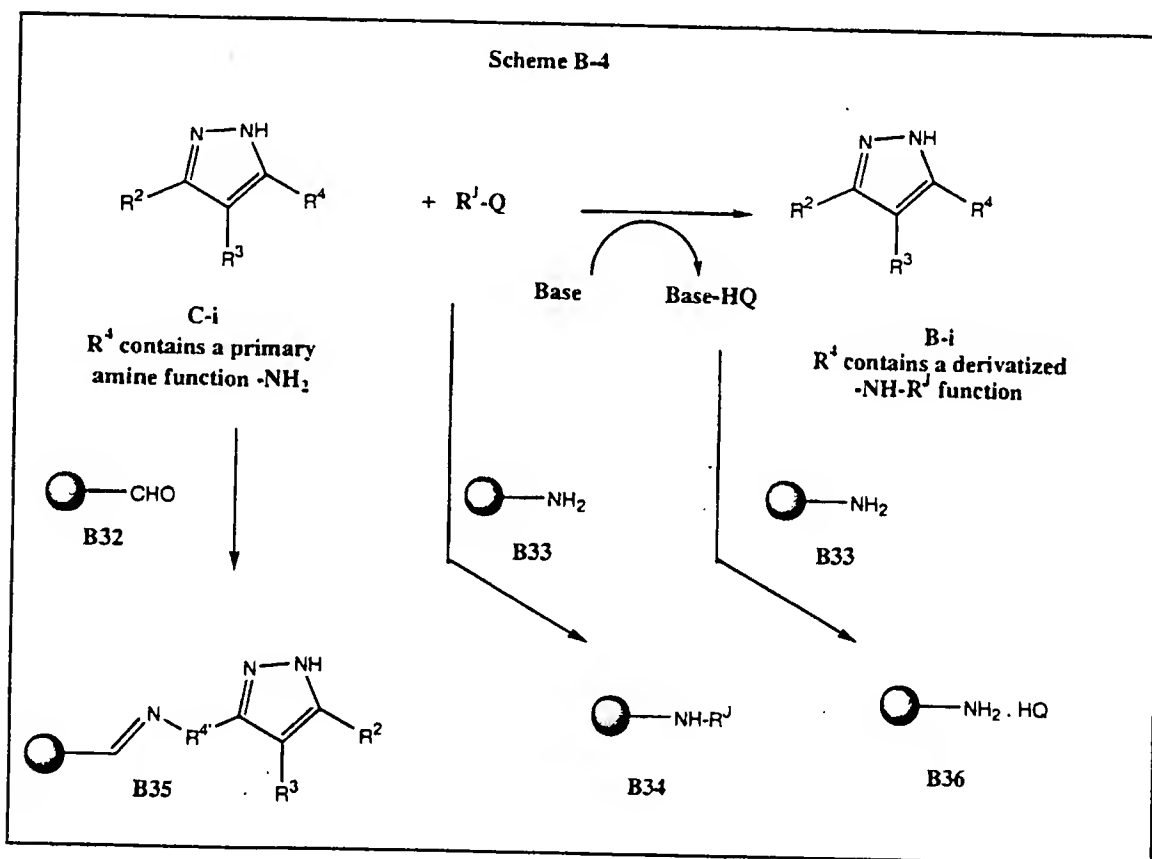
All communications between ChemLib and the robotics workstations are by ASCII files. These files are placed on a server by the ChemLib system that is accessible by

the robotics workstations. Reports generated by the robotics workstations are also placed on the server where the ChemLib system can read these files to record the data generated. Each robotics workstation consists of robotics hardware by Bohdan Automation, Inc. Mundelein, Illinois, and a PC currently running Microsoft Windows for Workgroup v3.11 and Ethernet software. The robotics workstation PC is logged into the network for one-way communication that allows the workstation to access the server for file access only.

#### General Scheme B4

Scaffold C-i with a primary amine functionality contained within the  $R^i$  substituent is reacted in spatially addressed, parallel array reaction block vessels with excess of electrophiles  $R^j$ -Q wherein Q is chloro, bromo, or an acid activating group including but not limited to N-hydroxysuccinimide.  $R^j$ -Q includes acid chlorides, alkyl chloroformates, sulfonyl chlorides, activated esters of carboxylic acids, activated carbamates, and isocyanates. Reaction of scaffold C-i with  $R^j$ -Q is effected in the presence of a tertiary amine base at room temperature in a mixture of a polar aprotic solvent and/or a halogenated solvent. As illustrated in Scheme B-4 the products of the general formulae B-i are isolated in purified form by addition of a carbonyl-functionalized resin B32 which covalently sequesters any unreacted primary amine scaffold C-i as resin-bound adduct B35, and also by the addition of a primary amine-functionalized resin B33 which covalently sequesters any remaining electrophile  $R^j$ -Q from each reaction mixture as

resin-bound adduct **B34**. Resin **B33** also sequesters the HQ byproduct from the reaction mixture by proton transfer from solution-phase **Base-HQ**. Incubation at room temperature, filtration, rinsing of the resin cake, and concentration of the filtrates affords purified products **B-i** filtered away from resin-bound adducts **B32**, **B33**, **B34**, **B35**, and **B36**.

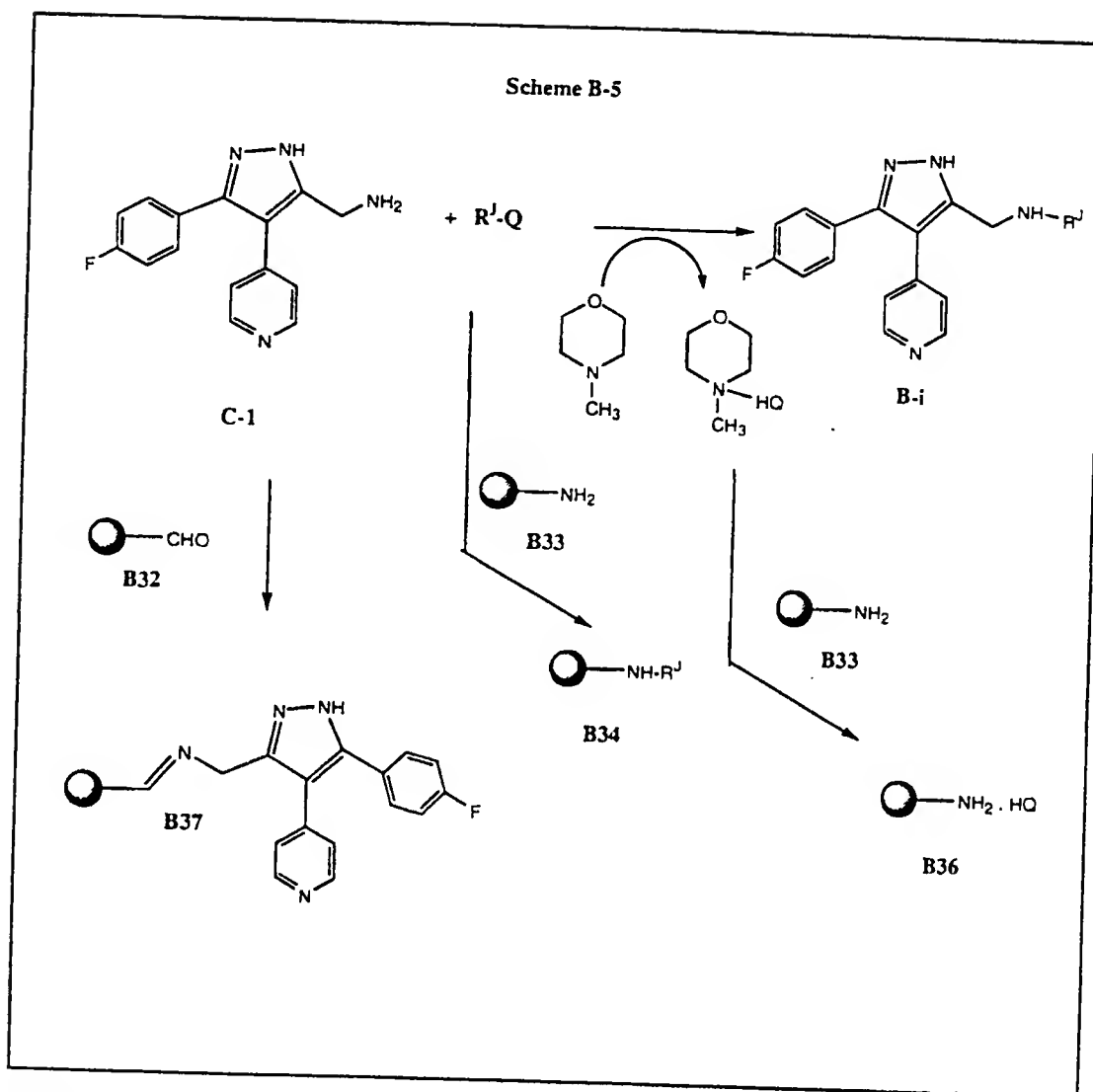


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Scheme B-5 specifically illustrates the derivatization of the primary amine-containing scaffold **C1** to afford the desired products **B-i** in a parallel array synthesis format. In a parallel array synthesis reaction block, individual reaction products are prepared in each of multiple reaction block vessels in a spatially

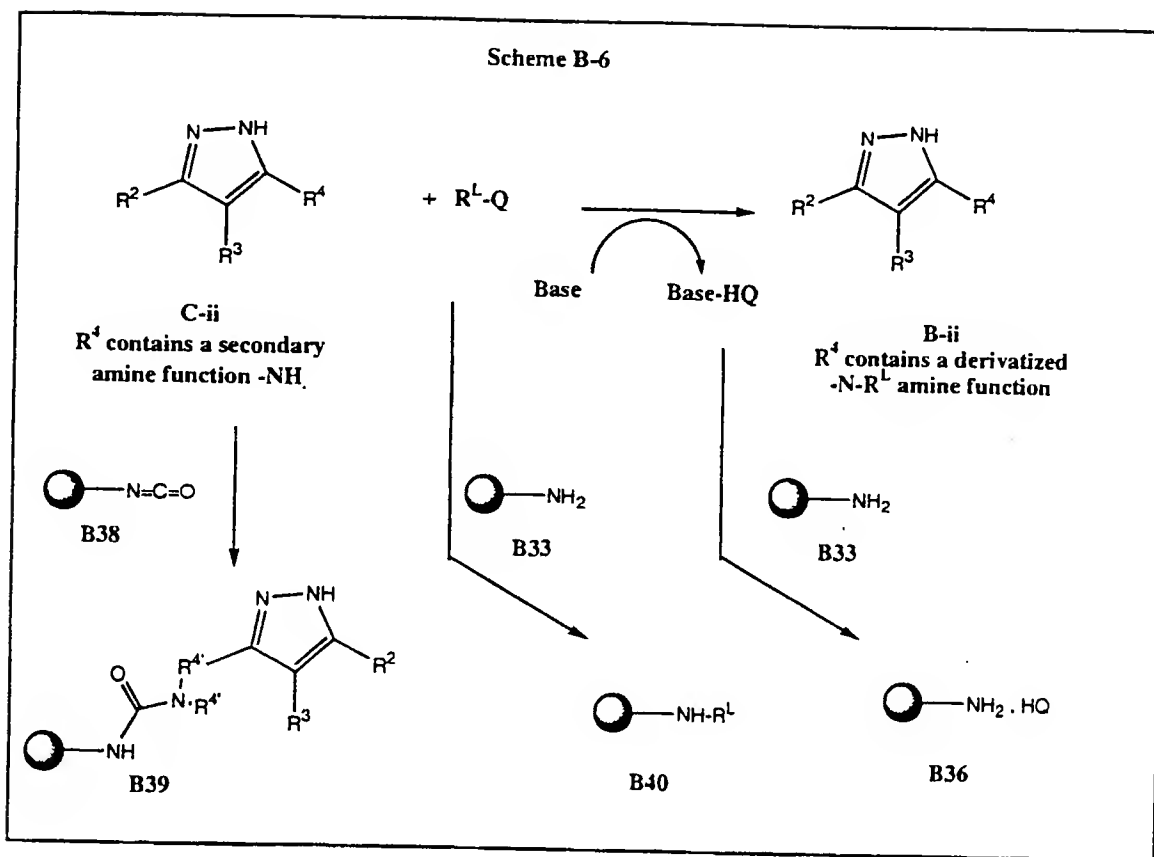
15

addressed format. A solution of the desired primary amine-containing scaffold **C1** (limiting amount,) in dimethylformamide (DMF) is added to the reaction vessels followed by a 4.0 fold stoichiometric excess solution of  
5 N-methylmorpholine in DMF. To each reaction vessel is then added the electrophiles: either a 2.0 fold stoichiometric excess when  $R^J$ -Q is an acid chloride or alkyl chloroformate, or a 1.5 fold stoichiometric excess when  $R^J$ -Q is a sulfonyl chloride, or a 1.25 fold  
10 stoichiometric excess when  $R^J$ -Q is an isocyanate. Excess electrophiles and N-methylmorpholine were used to effect more rapid and/or more complete conversion of scaffold **C1** to products B-0001-B-0048 compared to reactions that do not utilize stoichiometric excesses of electrophiles and  
15 N-methylmorpholine. The reaction mixtures are incubated at ambient temperature for 2-3 h. Each reaction vessel is then charged with a large excess (15-20 fold stoichiometric excess) of the amine-functionalized resin **B33** and the aldehyde-functionalized resin **B32**. The  
20 resin-charged reaction block is shaken vertically for 14-20 h on an orbital shaker at ambient temperature to allow optimum agitation of the resin-containing vessel mixtures. The excess electrophiles  $R^J$ -Q and any unreacted scaffold amine **C1** are removed from the reaction  
25 medium as insoluble adducts **B34** and **B37** respectively. In addition the N-methylmorpholine hydrochloride salt formed during the course of the reaction is also neutralized to its free base form by proton transfer reaction to the amine-functionalized resin **B33**. Simple filtration of the  
30 insoluble resin- adducts **B32**, **B33**, **B34**, **B36**, and **B37**, rinsing of the resin cake with dichloroethane, and evaporation of the filtrates affords the desired products **B-i** in purified form.



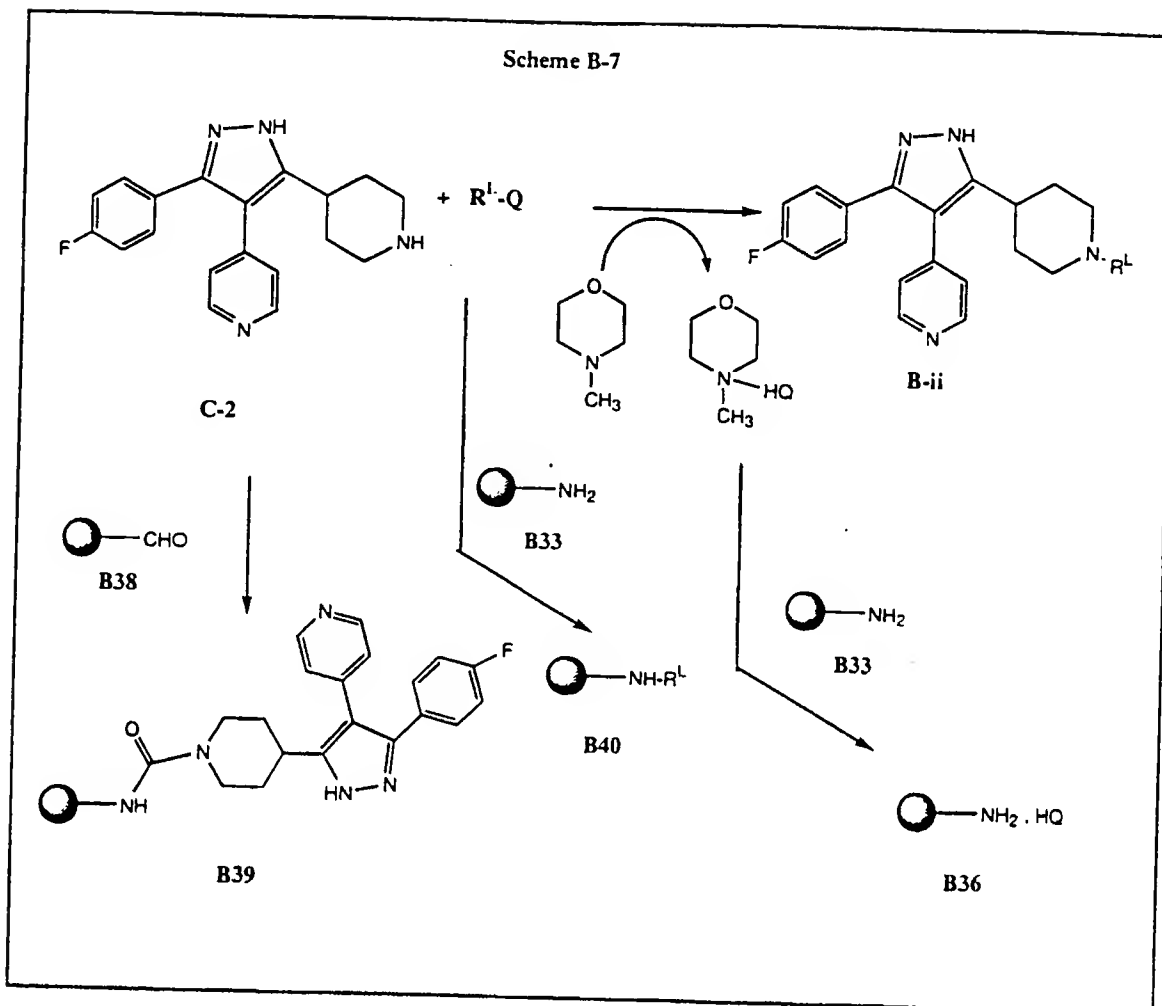
Scheme B-6 illustrates a general synthetic method involving the parallel array reaction of a scaffold C-ii containing a secondary amine functionality within the definition of the  $R^4$  substituent. Each reaction vessel is charged with the secondary amine-containing scaffold C-ii, followed by the introduction of a stoichiometric excess of an optionally unique electrophile  $R^L-Q$  into each vessel, wherein Q is chloro, bromo, or an acid activating group including but not limited to N-hydroxysuccinimide.  $R^L-Q$  includes acid chlorides, alkyl chloroformates,

sulfonyl chlorides, activated esters of carboxylic acids, activated carbamates, and isocyanates. Reaction of scaffold C-ii with  $R^L-Q$  is effected in the presence of tertiary amine base at room temperature or elevated  
5 temperature in a mixture of a polar aprotics solvent and/or a halogenated solvent. After solution-phase reactions have progressed to afford crude product mixtures in each vessel, the products  
B-ii are isolated in purified form by the addition of the  
10 isocyanate-functionalized resin B38 which covalently sequesters remaining secondary amine scaffold C-ii as resin-bound adduct B39, and also by the addition of the primary amine-functionalized resin B33 which covalently sequesters remaining electrophile  $R^L-Q$  from each reaction  
15 vessel as resin-bound adducts B40. Resin B33 also sequesters the HQ byproduct in each vessel as B36, formed by proton transfer from solution-phase Base-HQ. Incubation with these resins, either simultaneously or sequentially, followed by filtration, rinsing, and  
20 concentration of the filtrates affords purified products B-ii filtered away from resin-adducts B33, B36, B38, B39, and B40.



Scheme B-7 illustrates the conversion of the secondary-amine containing scaffold **C-2** to the desired products **B-ii**. In a parallel array synthesis reaction block, individual reaction products are prepared in each of 48 multiple reaction block vessels. A solution of the scaffold **C-2** (limiting amount) in dimethylformamide (DMF) is added to the reaction vessels followed by a 4.0-fold stoichiometric excess solution of N-methylmorpholine in DMF. To each reaction vessel is then added an electrophile  $R^L-Q$  as a dichloroethane (DCE) solution: either a 2.0 fold stoichiometric excess is used when  $R^L-Q$  is an acid chloride or alkyl chloroformate, or a 1.5 fold stoichiometric excess when  $R^L-Q$  is a sulfonyl chloride, or a 1.25 fold stoichiometric excess when  $R^L-Q$  is an isocyanate. The reaction mixtures are incubated at

ambient temperature for 2-6 h. Each reaction vessel is then charged with a large excess (15-20 fold stoichiometric excess) of the amine-functionalized resin **B33** and the isocyanate-functionalized resin **B32**. The resin-charged reaction block is shaken vertically for 14-20 h on an orbital shaker at ambient temperature to allow optimum agitation of the resin-containing vessel mixtures. The excess electrophiles  $R^L-Q$  and unreacted scaffold amine **C-2** are removed from the reaction medium as insoluble adducts **B40** and **B39**, respectively. Resin **B33** also sequesters the HQ byproduct in each vessel as **B36**, formed by proton transfer from solution-phase Base-HQ. Incubation with these resins, followed by filtration and rinsing with solvent mixtures of DMF and/or DCE, affords purified product solutions in collection vials filtered away from resin-adducts **B33**, **B36**, **B38**, **B39**, and **B40**. Concentration of filtrates affords purified products **B-ii**.

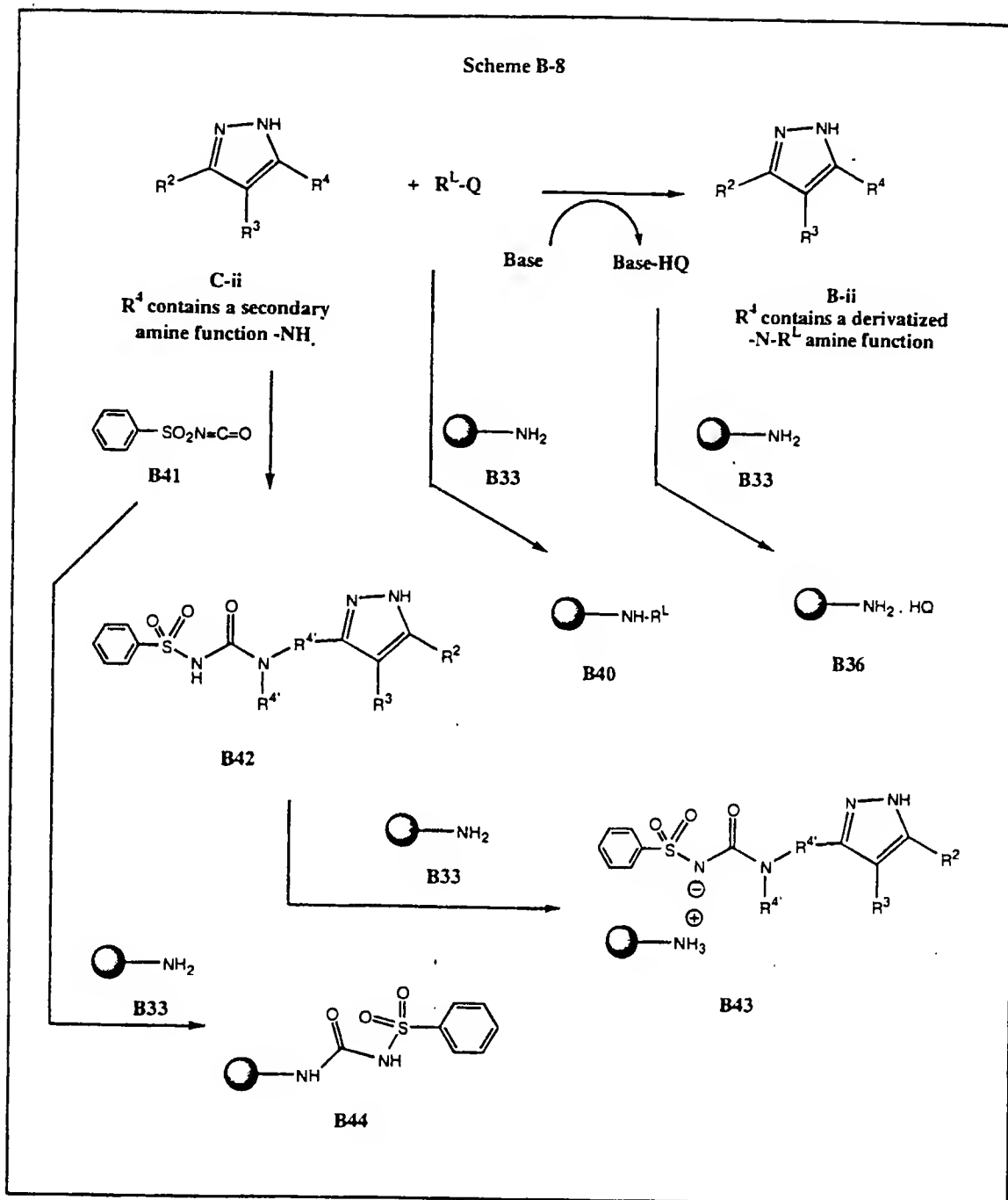


5 Scheme B-8 illustrates another general synthetic method involving the parallel array reaction of a scaffold C-ii containing a secondary amine functionality within the definition of the  $R^4$  substituent. Each reaction vessel is charged with the secondary amine-containing scaffold C-ii, followed by the introduction of a stoichiometric excess of an optionally unique electrophile  $R^L-Q$  into each vessel. Reaction of scaffold C-ii with  $R^L-Q$  is effected in the presence of tertiary amine base at room temperature or elevated temperature in a mixture of a polar aprotic solvent and/or a halogenated solvent.

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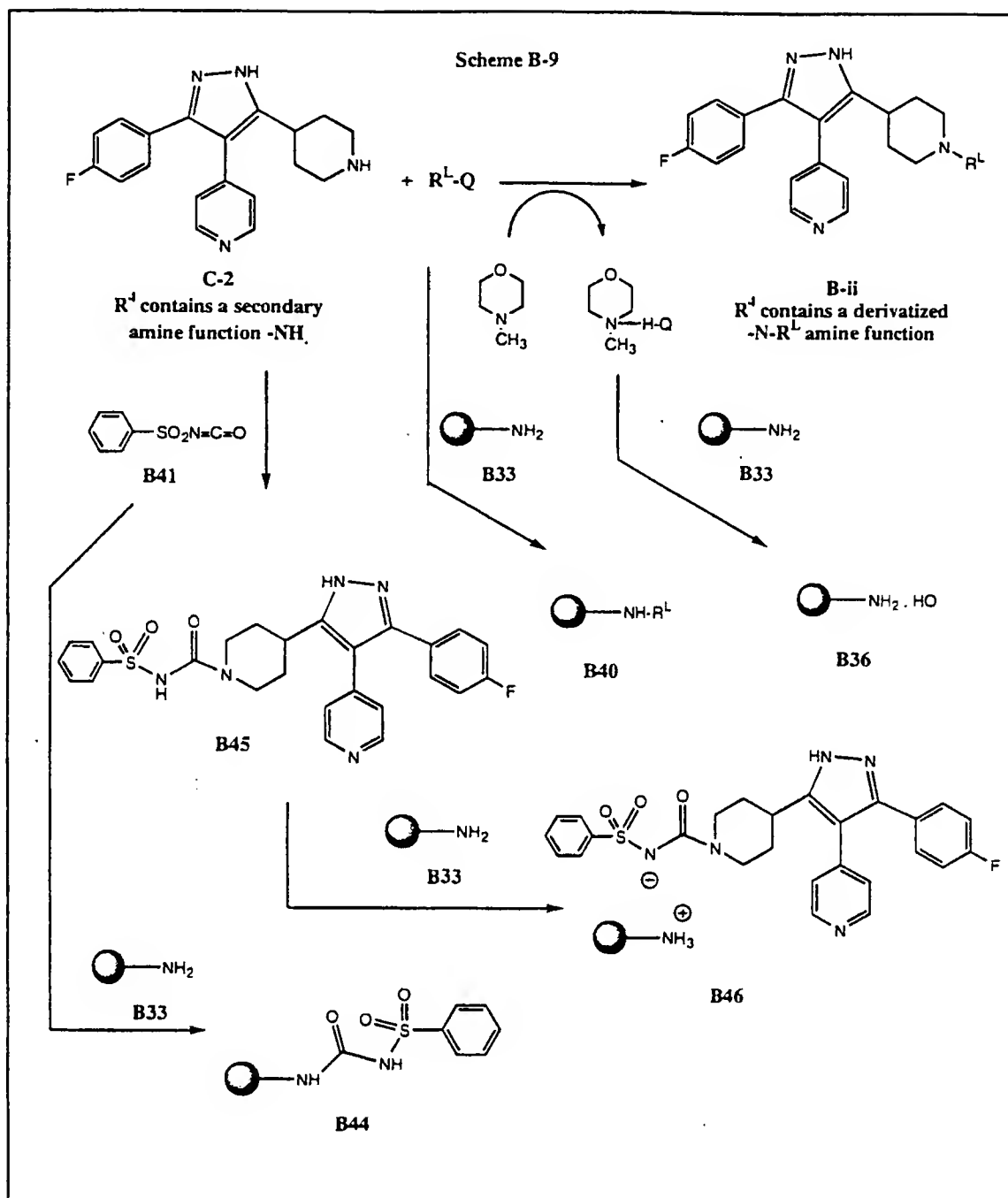
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Excess electrophiles and N-methylmorpholine are used to effect more rapid and/or more complete conversion of scaffold **C-ii** to products **B-ii** compared to reactions that do not utilize stoichiometric excesses of electrophiles and N-methylmorpholine. The reaction mixtures are incubated at ambient temperature for 2-8 h. Each reaction vessel is then charged with the sequestration-enabling reagent phenylsulfonylisocyanate **B41**. This reagent **B41** reacts with remaining secondary amine scaffold **C-ii**, converting **C-ii** to the *in situ*-derivatized compound **B42**. Subsequent incubation of these vessel mixtures with a large excess (15-20 fold stoichiometric excess) of the amine-functionalized resin **B33** sequesters the solution-phase species  $R^L-Q$ , **HQ**, **B41**, and **B42** as the resin-bound adducts **B40**, **B36**, **B44**, and **B43**, respectively. The resin-charged reaction block is shaken vertically for 14-20 h on an orbital shaker at ambient temperature to allow optimum agitation of the resin-containing vessel mixtures. Filtration of the insoluble resin- adducts **B33**, **B36**, **B40**, **B43** and **B44** and subsequent rinsing of the vessel resin-bed with DMF and/or DCE affords filtrates containing the purified products **B-ii**. Concentration of the filtrates affords the purified products **B-ii**.



Scheme B-9 illustrates the method of Scheme B-8 using scaffold **C-2**. A solution of the scaffold **C-2** (limiting

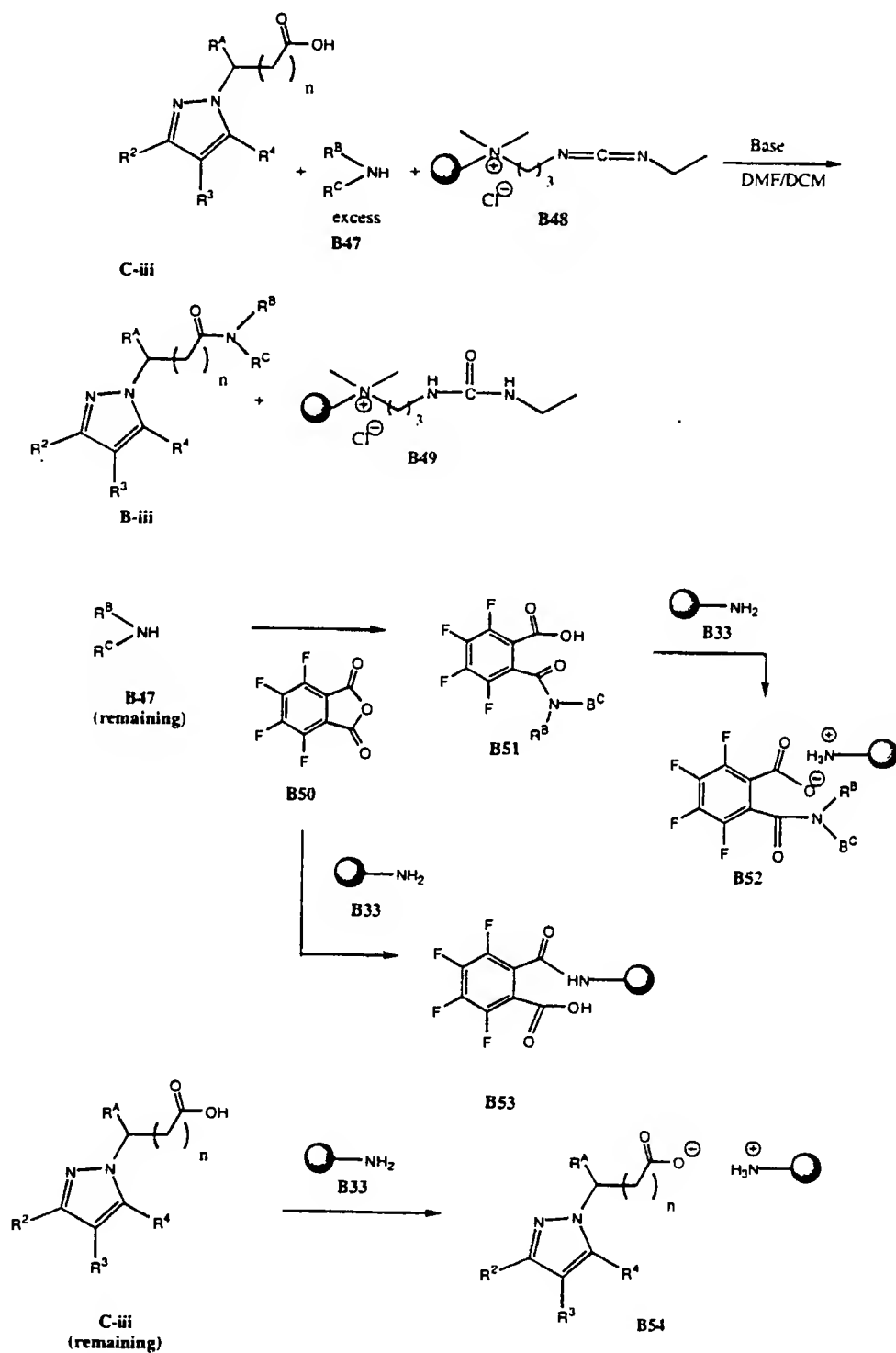
amount) in dimethylformamide (DMF) is added to the reaction vessels followed by a 4.0-fold stoichiometric excess solution of N-methylmorpholine in DMF. To each reaction vessel is then added an electrophile  $R^L-Q$  as a  
5 dichloroethane (DCE) solution: either a 2.0 fold stoichiometric excess is used when  $R^L-Q$  is an acid chloride or alkyl chloroformate, or a 1.5 fold stoichiometric excess when  $R^L-Q$  is a sulfonyl chloride, or a 1.25 fold stoichiometric excess when  $R^L-Q$  is an  
10 isocyanate. The reaction mixtures are incubated at ambient temperature for 2-6 h. After solution-phase reactions have progressed to afford crude product mixtures, each reaction vessel is then charged with a dichloroethane solution of the sequestration-enabling  
15 reagent phenylsulfonylisocyanate **B41**. This reagent **B41** reacts with remaining secondary amine scaffold **C-2**, converting **C-2** to the *in situ*-derivatized compound **B45**. Subsequent incubation of these vessel mixtures with a large excess (15-20 fold stoichiometric excess) of the  
20 amine-functionalized resin **B33** sequesters the solution-phase species  $R^L-Q$ , **HQ**, **B41**, and **B45** as the resin-bound adducts **B40**, **B36**, **B44**, and **B46**, respectively. The resin-charged reaction block is shaken vertically for 20 h on an orbital shaker at ambient temperature to allow optimum  
25 agitation of the resin-containing vessel mixtures. Filtration of the insoluble resin- adducts **B33**, **B36**, **B40**, **B44**, and **B46** and subsequent rinsing of the vessel resin-bed with DCE affords filtrates containing the purified products **B-ii**. Concentration of the filtrates affords  
30 the purified products **B-ii**.



Another general method for the parallel array reaction block synthesis is illustrated in Scheme B-10 for the derivatization of the carboxylic acid-containing scaffold

**C-iii.** Scaffold **C-iii** with a free carboxylic acid functionality is reacted in spatially addressed, parallel array reaction block vessels with excesses of optionally different primary or secondary amines **B47** in the presence of the polymer-bound carbodiimide reagent **B48** and a tertiary amine base in a mixture of a polar aprotic solvent and/or a halogenated solvent. After filtration of each crude vessel product mixture away from resins **B48** and **B49**, each reaction mixture is purified by treatment with the sequestration-enabling-reagent **B50** (tetrafluorophthalic anhydride). The reagent **B50** reacts with remaining excess amine **B47** to afford the *in situ*-derivatized intermediates **B51** which contain carboxylic acid molecular recognition functionality. Subsequent incubation of each reaction mixture with a 15-20-fold stoichiometric excess of the primary amine-functionalized resin **B33** sequesters **B51**, **B50**, and any remaining acid scaffold **C-iii** as resin-bound adducts **B52**, **B53**, and **B54**, respectively. Filtration of solution-phase products **B-iii** away from these resin-bound adducts and rinsing of the resin beds with a polar aprotic solvent and/or halogenated solvent affords filtrates containing purified products **B-iii**. Concentration of the filtrates affords purified **B-iii**.

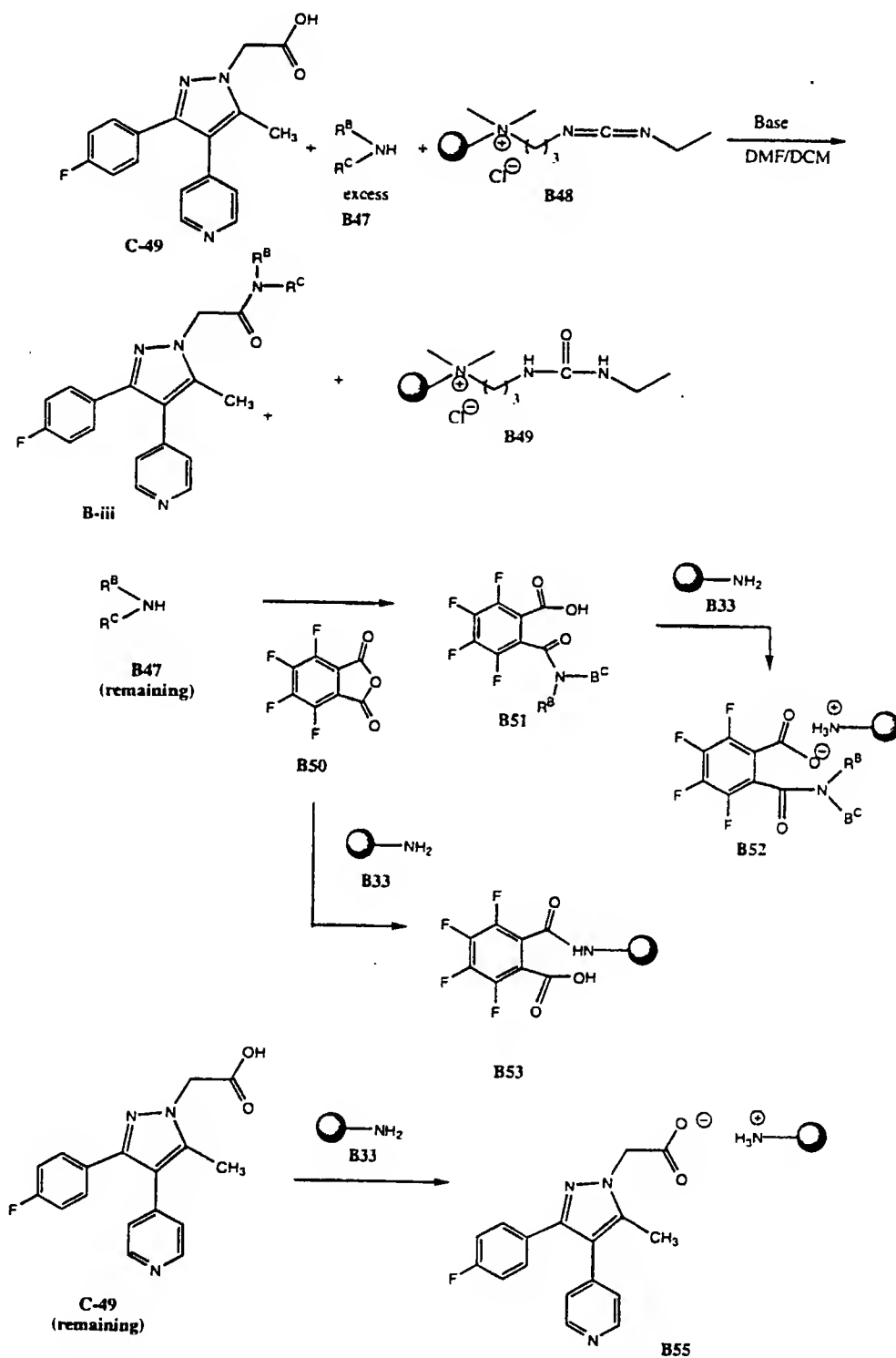
Scheme B-10



Scheme 'B-11 illustrates the conversion of the acid containing scaffold **C-49** to the desired amide products **B-iii** in a parallel synthesis format. A limiting amount of the scaffold **C-49** is added as a solution in  
5 dimethylformamide to each reaction vessel containing the polymer bound carbodiimide reagent **B48** (5 fold stoichiometric excess). A solution of pyridine (4 fold stoichiometric excess) in dichloromethane is added to this slurry, followed by addition of an excess amount of  
10 a dimethylformamide solution of a unique amine **B47** (1.5 fold stoichiometric excess) to each vessel. The parallel reaction block is then agitated vertically on an orbital shaker for 16-18 h at ambient temperature and filtered to separate the solution phase product mixture away from  
15 resin-bound reagent **B48** and resin-bound reagent byproduct **B49**. The resulting solutions (filtrates) containing a mixture of the desired amide products **B-iii**, excess amines **B47** and any unreacted acid containing scaffold **C-49**, are treated with tetrafluorophthalic anhydride **B50**.  
20 **B50** converts the excess amines **B47** in each filtrate vessel to its respective sequesterable half acid form **B51**. After two h incubation time, an excess of the amine-functionalized resin **B33** and dichloromethane solvent are added to each reaction vessel. The amine-containing  
25 resin **B33** converts **B51**, any remaining **B50**, and any remaining **C-49** to their resin-bound adducts **B52**, **B53**, and **B55**, respectively. The resin-charged reaction block is shaken vertically for 16 h on an orbital shaker at ambient temperature to allow optimum agitation of the  
30 resin-containing vessel mixtures. Filtration of the insoluble resin- adducts **B33**, **B52**, **B53**, and **B55** and subsequent rinsing of the vessel resin-bed with

dimethylformamide affords filtrates containing the purified products **B-iii**. Concentration of the filtrates affords the purified products **B-iii**.

Scheme B-11



Although Schemes B-1 through B-11 describe the use of parallel array chemical library technology to prepare compounds of general formulae **B-i**, **B-ii**, and **B-iii**, it is noted that one with ordinary skill in the art of classical synthetic organic chemistry would be able to prepare **B-i**, **B-ii**, and **B-iii** by conventional means (one compound prepared at a time in conventional glassware and purified by conventional means such as chromatography and/or crystallization).

A general synthesis of pyridylpyrazole scaffolds **C-i**, **C-ii**, and **C-iii** is depicted in Scheme C-1.

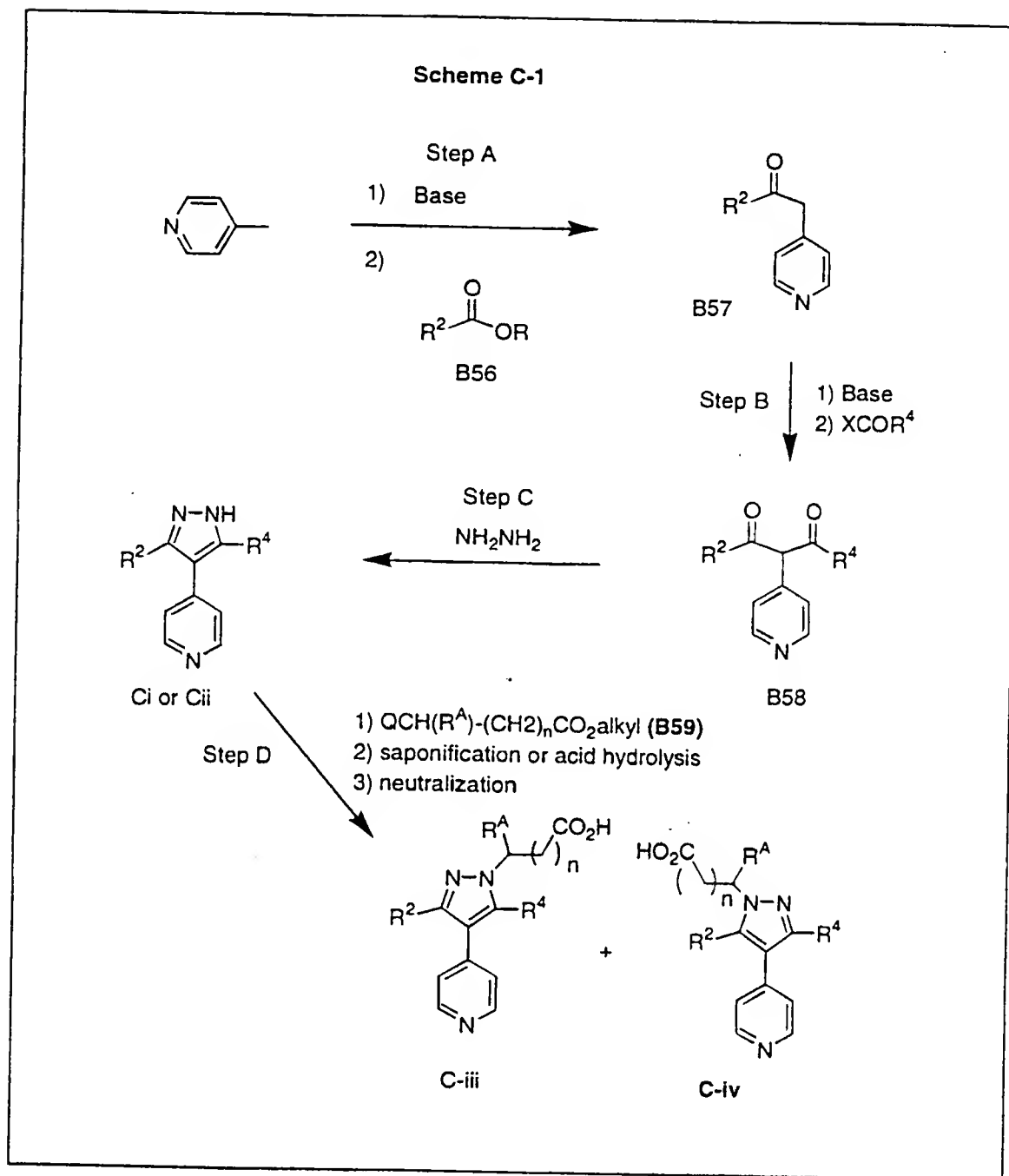
Step A: Picoline is treated with a base chosen from but not limited to n-butyllithium (n-BuLi), lithium di-isopropylamide (LDA), lithium hexamethyldisilazide (LiHMDS), potassium t-butoxide (tBuOK), or sodium hydride (NaH) in an organic solvent such as tetrahydrofuran (THF), diethyl ether, t-butyl methyl ether, t-BuOH or dioxane from -78 °C to 50 °C for a period of time from 10 minutes to 3 hours. The metallated picoline solution is then added to a solution of ester **B56**. The reaction is allowed to stir from 30 minutes to 48 hours during which time the temperature may range from -20 °C to 120 °C. The mixture is then poured into water and extracted with an organic solvent. After drying and removal of solvent the pyridyl monoketone **B57** is isolated as a crude solid which can be purified by crystallization and/or chromatography.

Step B: A solution of the pyridyl monoketone **B57** in ether, THF, tBuOH, or dioxane is added to a base chosen from but not limited to n-BuLi, LDA, LiHMDS, tBuOK, or NaH contained in hexane, THF, diethyl ether, t-butyl methyl ether, or t-BuOH from -78 °C to 50 °C for a period of time from ranging from 10 minutes to 3 hours. An appropriately substituted activated ester or acid halide derived from  $R^4\text{-CO}_2\text{H}$  is then added as a solution in THF, ether, or dioxane to the monoketone anion of **B57** while the temperature is maintained between -50 °C and 50 °C. The resulting mixture is allowed to stir at the specified temperature for a period of time from 5 minutes to three hours. The resulting pyridyl diketone intermediate **B58** is utilized without purification in Step C.

Step C: The solution containing the pyridyl diketone **B58** is quenched with water and the pH is adjusted to between 4 and 8 utilizing an inorganic or organic acid chosen from HOAc,  $\text{H}_2\text{SO}_4$ , HCl, or  $\text{HNO}_3$ . The temperature during this step is maintained between -20 °C and room temperature. Hydrazine or hydrazine hydrate was then added to the mixture while maintaining the temperature between -20 °C and 40 °C for a period of 30 minutes to three hours. The mixture is then poured into water and extracted with an organic solvent. The pyridyl pyrazole **C-i** or **C-ii** is obtained as a crude solid which is purified by chromatography or crystallization.

Step: D In some cases the pyridyl pyrazole **C-i** or **C-ii** is alkylated with  $\text{Q-C(R}^A\text{)}-(\text{CH}_2)_n\text{CO}_2\text{alkyl}$  wherein Q is halogen. **C-i** or **C-ii** is treated with a base chosen from NaH, NaOEt, KOtBu, or  $\text{NEt}_3$  in an organic solvent such as THF, methylene chloride, dioxane, or DMF at temperatures

between -20 °C and 150 °C and reaction times between 30 minutes and 12 hours. The resulting alkylated pyridyl pyrazole ester is then hydrolyzed to the acid by treatment with NaOH or LiOH in aqueous/alcohol solvent mixtures or in THF/water solvent mixtures. Alternatively, the ester function is removed by treatment with an organic or inorganic acid if the alkyl residue is *t*-butyl. Acidification, followed by extraction with an organic solvent affords **C-iii** which may be purified by chromatography or crystallography. In some cases, regioisomeric alkylated products **C-iv** are also formed. The desired **C-iii** can be separated away from **C-iv** by chromatographic purification or by fractional crystallization.



5 A synthesis of pyridylpyrazole scaffold **C-1** is depicted in Scheme C-2.

Step A:

Picoline is added to a solution of LiHMDS in THF at room temperature over a time period ranging from 30 minutes to 1 hour. The resulting solution is stirred for an additional 30 minutes to 1 hour at room temperature.

5 This solution is then added to neat ethyl p-fluorobenzoate **B60** at room temperature over 1-2 h. The mixture is then allowed to stir at room temperature for 16-24 h. Equal portions of water and ethyl acetate are then added to the reaction and the mixture is partitioned  
10 in an extraction funnel. The organic layer is dried, filtered, and evaporated to give an oily solid. Hexanes are then added and the solid is filtered and washed with cold hexanes leaving the pyridyl monoketone **B61** for use in Step B.

15 Step B:

The pyridyl monoketone **B61** is added as a solution in THF to a flask maintained at room temperature which contains t-BuOK in a THF/ t-BuOH cosolvent. A yellow precipitate forms and stirring at room temperature is continued for  
20 1-3 h. After this time, N-Cbz-protected glycine N-hydroxysuccinimide **B62** is added dropwise at room temperature as a solution in THF over 1-3 h. This solution, containing crude diketone **B63**, is used directly in Step C.

25 Step C: The solution from step C is treated with water and the pH is adjusted to between 6 and 7 with acetic acid. Hydrazine hydrate is then added dropwise to the mixture as a solution in water over 30 minutes to 1h at room temperature. Water and ethyl acetate are then added  
30 to the flask and the mixture is then partitioned in a separatory funnel. The organic layer is dried, filtered, and evaporated to give a crude oil which is purified by

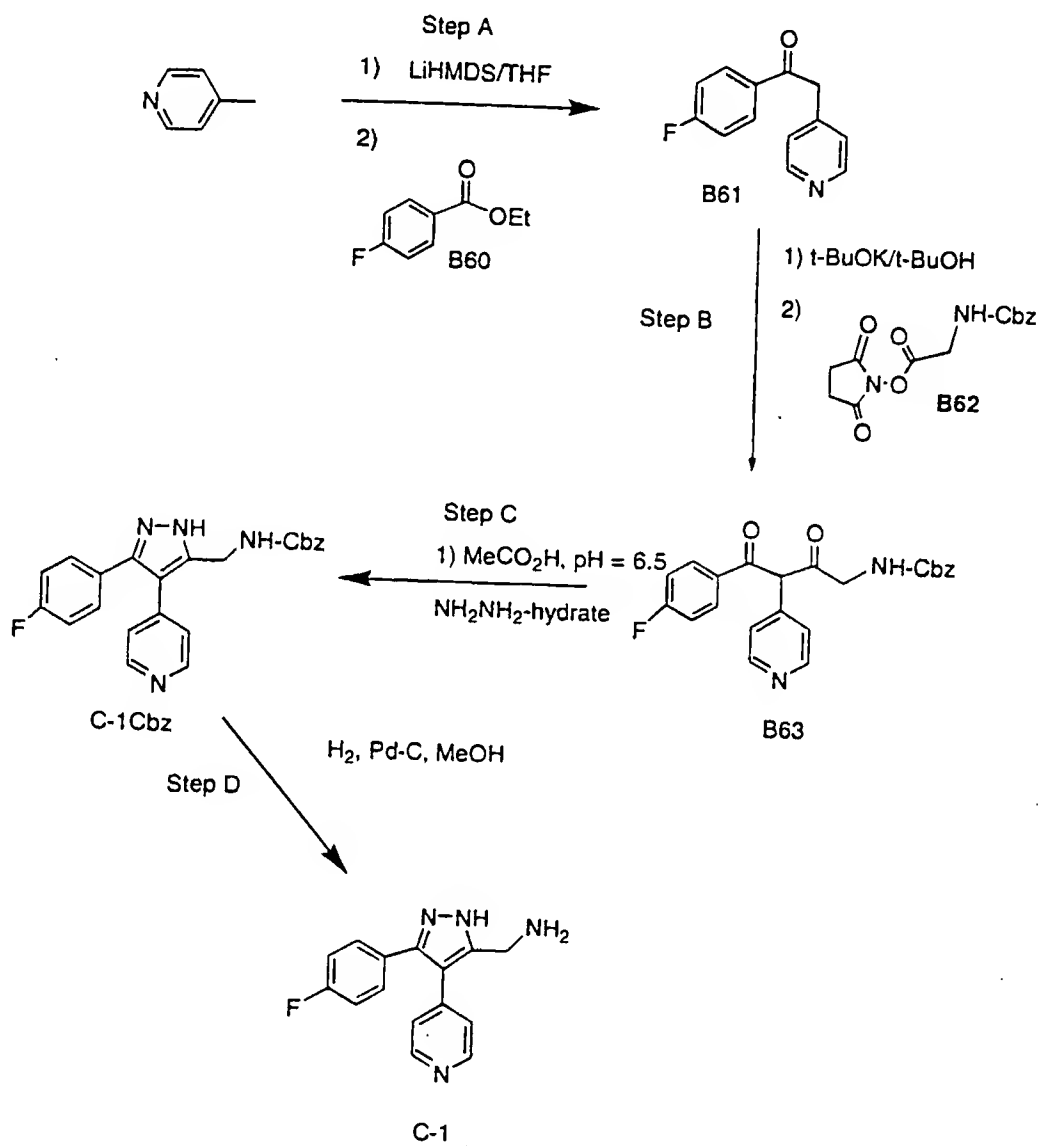
silica gel chromatography, giving rise to purified **C-1Cbz**.

Step: D

- 5 The Cbz protecting group contained in compound **C-1Cbz** is cleaved using hydrogen gas under pressure and Pd-C in methanol solvent. The resulting amine **C-1** is obtained by filtration and concentration.

567

Scheme C-2



A number of pyridyl pyrazole scaffolds of type C-v are prepared as shown in Scheme C-3.

Step A: Picoline is treated with a base chosen from but not limited to *n*-BuLi, LDA, LiHMDS, *t*BuOK, or NaH in an organic solvent such as THF, ether, *t*-BuOH or dioxane from -78 °C to 50 °C for a period of time from 10 minutes to 3 hours. The metallated picoline solution is then added to a solution of an appropriately activated ester analog of a carboxylic acid CbzNR<sup>H</sup>-(CH<sub>2</sub>)<sub>n</sub>CR<sup>F</sup>(R<sup>G</sup>)-CO<sub>2</sub>H or BocNR<sup>H</sup>-(CH<sub>2</sub>)<sub>n</sub>CR<sup>F</sup>(R<sup>G</sup>)-CO<sub>2</sub>H, preferably but not limited to the N-hydroxysuccinimide **B64**. The reaction is allowed to stir from 30 minutes to 48 hours during which time the temperature may range from -20 °C to 120 °C. The mixture is then poured into water and extracted with an organic solvent. After drying and removal of solvent the pyridyl monoketone **B65** is isolated as a crude solid which can be purified by crystallization and/or chromatography.

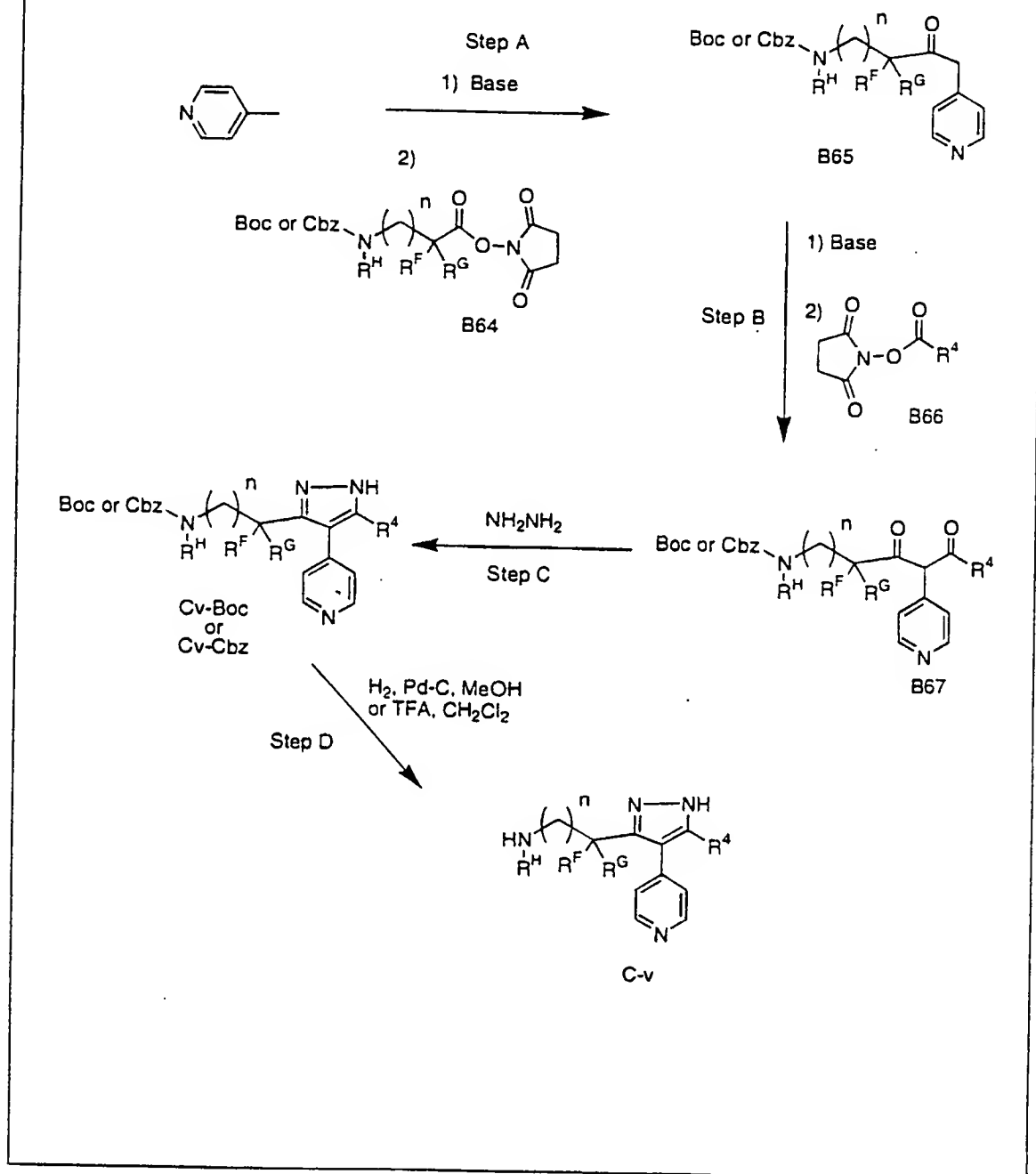
Step B: A solution of the pyridyl monoketone **B65** in ether, THF, *t*BuOH, or dioxane is added to a base chosen from but not limited to *n*-BuLi, LDA, LiHMDS, *t*BuOK, or NaH contained in hexane, THF, ether, dioxane, or *t*BuOH from -78 °C to 50 °C for a period of time from 10 minutes to 3 hours. The anion sometimes precipitates as a yellow solid. An appropriately substituted activated ester such as the N-hydroxysuccinimide **B66** is then added as a solution in THF, ether, or dioxane to the monoketone anion while the temperature is maintained between -50 °C and 50 °C. The resulting mixture is allowed to stir at the specified temperature for a period of time from ranging from 5 minutes to 3 hours. The resulting pyridyl diketone intermediate **B67** is utilized without further purification in Step C.

Step C: The solution containing the pyridyl diketone **B67** is quenched with water and the pH is adjusted to between 4 and 8 utilizing an inorganic or organic acid chosen from HOAc, H<sub>2</sub>SO<sub>4</sub>, HCl, or HNO<sub>3</sub>. The temperature during this step is maintained between -20 °C and room temperature. Hydrazine or hydrazine hydrate is then added to the mixture while maintaining the temperature between -20 °C and 40 °C for a period of 30 minutes to three hours. The mixture is then poured into water and extracted with an organic solvent. The pyridyl pyrazole **C-vBoc** or **C-vCbz** is obtained as a crude solid which is purified by chromatography or crystallization.

15 Step: D

The carbamate protecting groups from **C-vBoc** or **C-vCbz** are removed to afford the scaffolds **C-v** containing either a free primary amine (R<sup>H</sup> is hydrogen) or a free secondary amine (R<sup>H</sup> not equal to hydrogen). The Boc protecting carbamate groups are cleaved utilizing 1:1 trifluoroacetic acid (TFA)/methylene chloride at room temperature for several hours. The CBZ carbamate protecting groups are cleaved using hydrogen gas under pressure and Pd-C in an alcoholic solvent. The resulting amines **C-v** are then optionally crystallized or purified by chromatography.

Scheme C-3



The synthesis of scaffolds **C-vi** is accomplished as shown in Scheme C-4.

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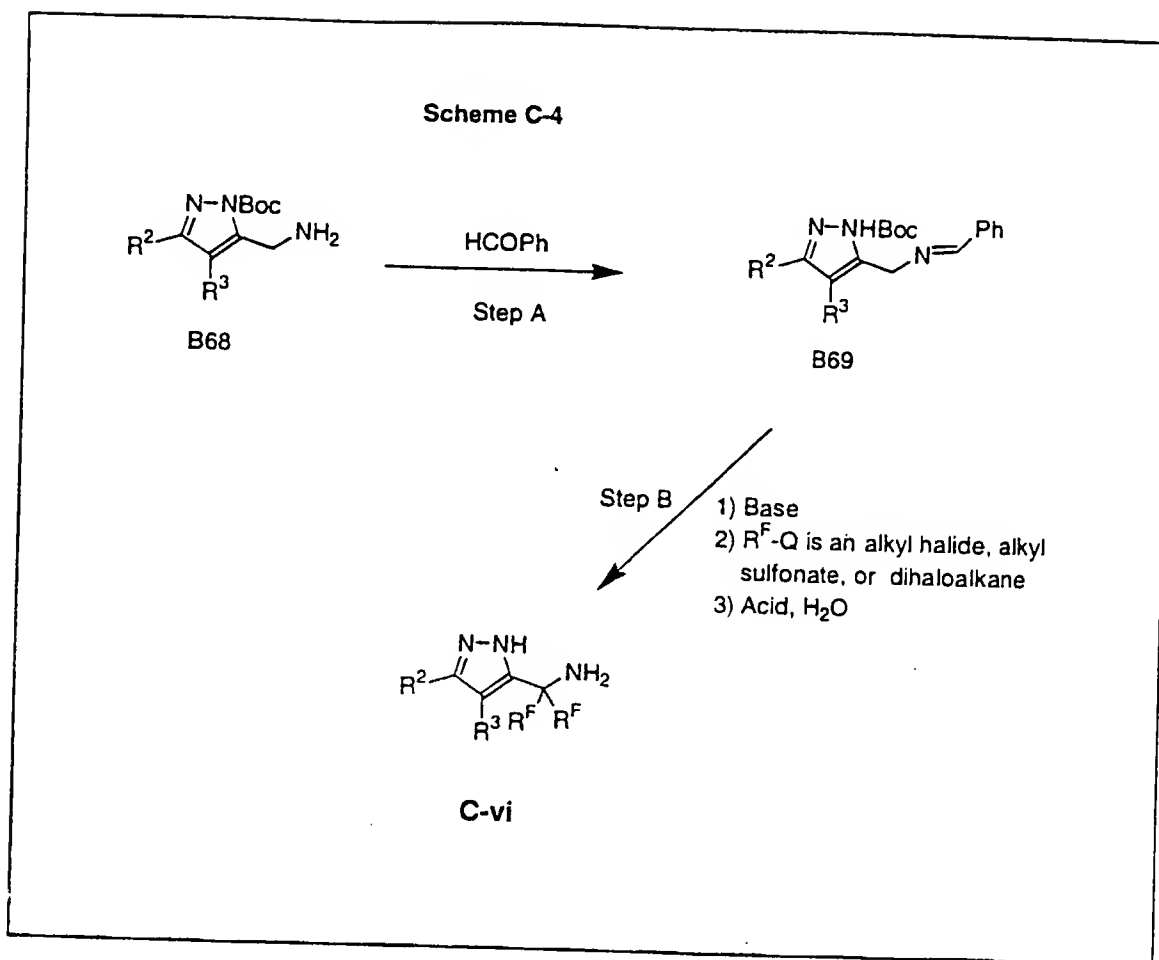
Step A:

A Boc protected pyridylpyrazole **B68** is treated with benzaldehyde in methylene chloride at room temperature in the presence of a drying agent for a period of time ranging from 1-24 h. Solvent is then evaporated and the resulting imine **B69** is used in step B without further purification.

Step B:

15 The pyridylpyrazole imine **B69** is dissolved in THF and stirred under nitrogen at temperatures ranging from -78 to -20 °C. A base such as LDA, *n*-BuLi, or LiHMDS is added dropwise to the mixture which is then stirred for an additional 10 minutes to 3 h. Two-five equivalents of an alkylating agent  $R^F-Q$  are then added to the mixture and stirring is continued for several hours. The mixture is then quenched with acid and allowed to warm to room temperature and stirred several hours until cleavage of the Boc and the imine functions is complete. The pH is adjusted to 12 and then the mixture is extracted with an organic solvent, which is dried and evaporated. The crude pyridylpyrazole is then crystallized and/or chromatographed to give **C-vi**.

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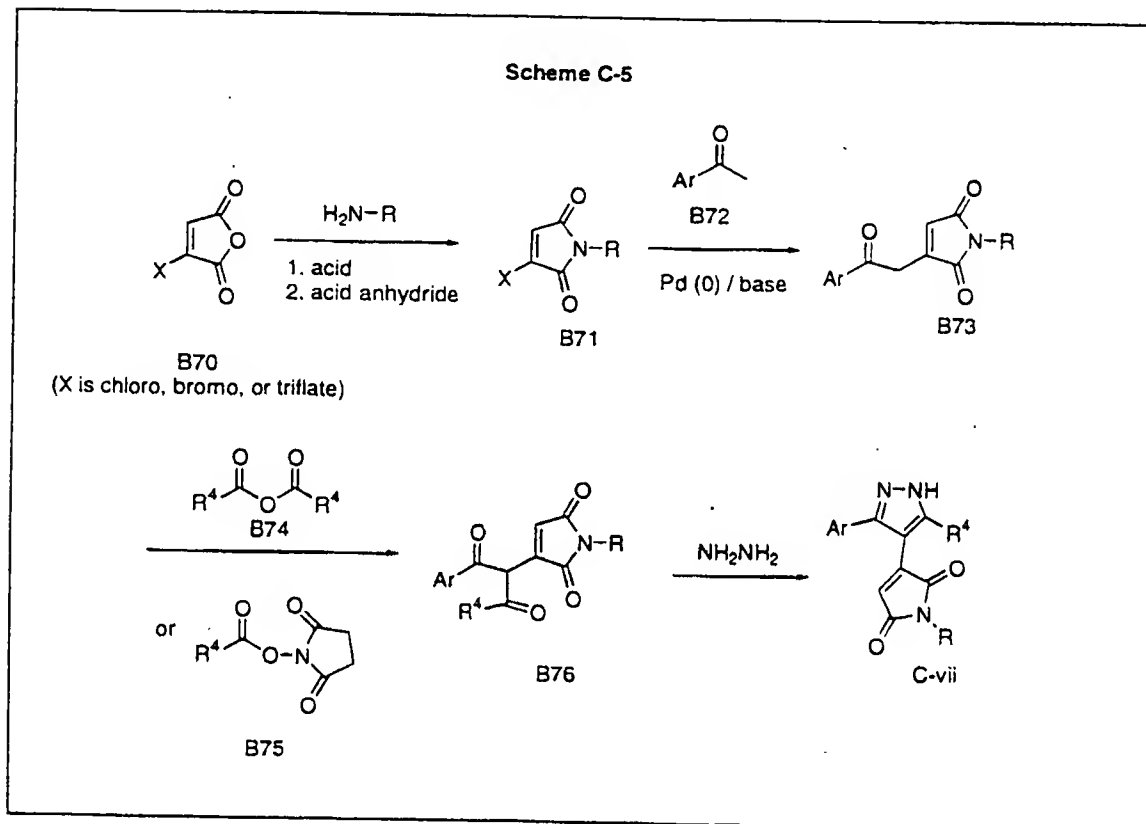


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The synthesis of maleimide-containing scaffolds **C-vii** is accomplished as shown in Scheme C-5.

The maleimide pyrazole scaffolds **C-vii** are synthesized as depicted in scheme C-5. Condensation reaction of a primary amine  $\text{H}_2\text{N-R}$  with a maleic anhydride **B70** that is substituted at position 3 with either a bromo, chloro, or triflate group generates compound **B71**. The formed maleimide derivative **B71** then reacts with an acetophenone derivative **B72** in the presence of a  $\text{Pd}(0)$

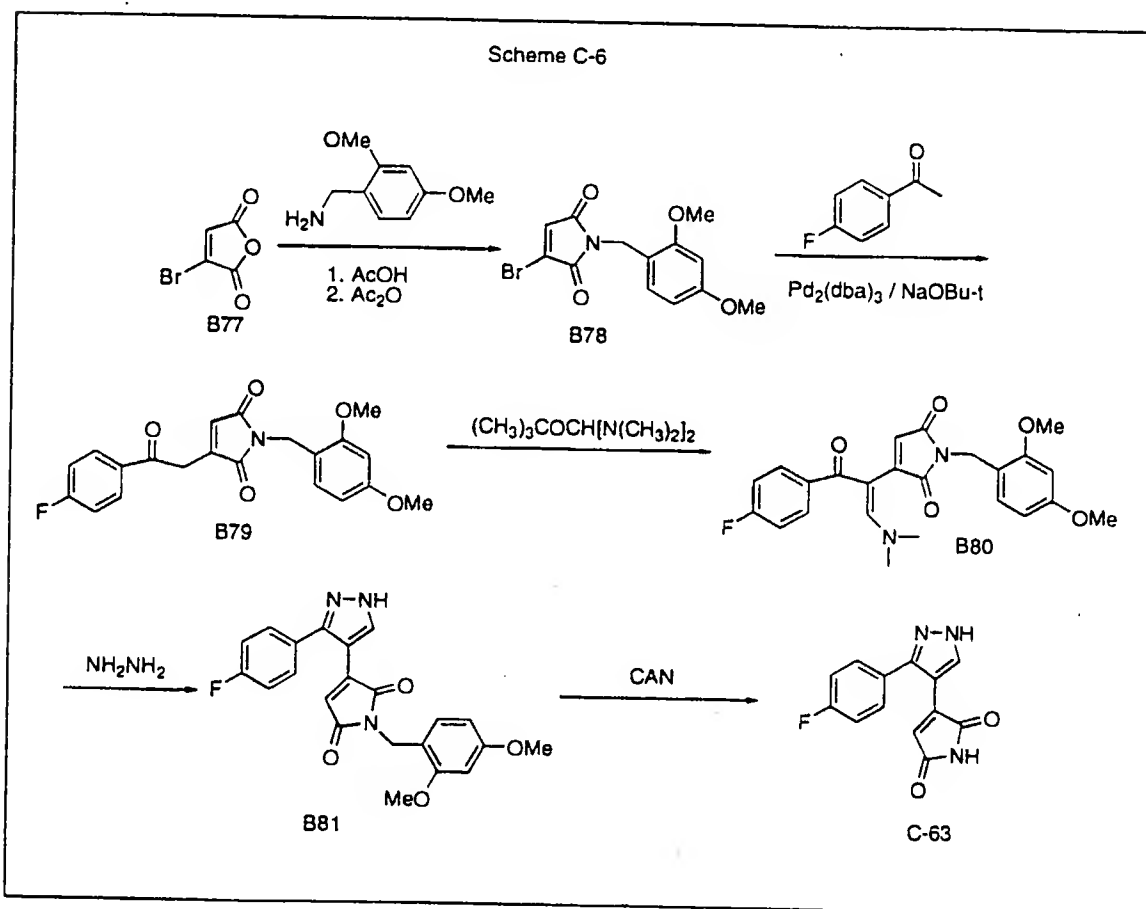
catalyst and base to afford compound **B73**. The methylene position of **B73** is then acylated with an acid anhydride **B74** or an activated acid ester **B75**, forming the di-ketone derivative **B76**. The di-ketone **B76** condenses with hydrazine to afford the desired maleimide pyrazole scaffold **C-vii**.



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Scheme C-6 illustrates the synthesis of the maleimide pyrazole scaffold **C-63** wherein  $\text{R}^4$  is hydrogen. The synthesis starts with the condensation reaction of bromomaleic anhydride **B77** with 2, 4-dimethoxybenzylamine in acetic acid and acetic anhydride, giving rise to intermediate **B78**. The maleimide **B78** is then treated with 4'-fluoroacetophenone in the presence of catalytic amount

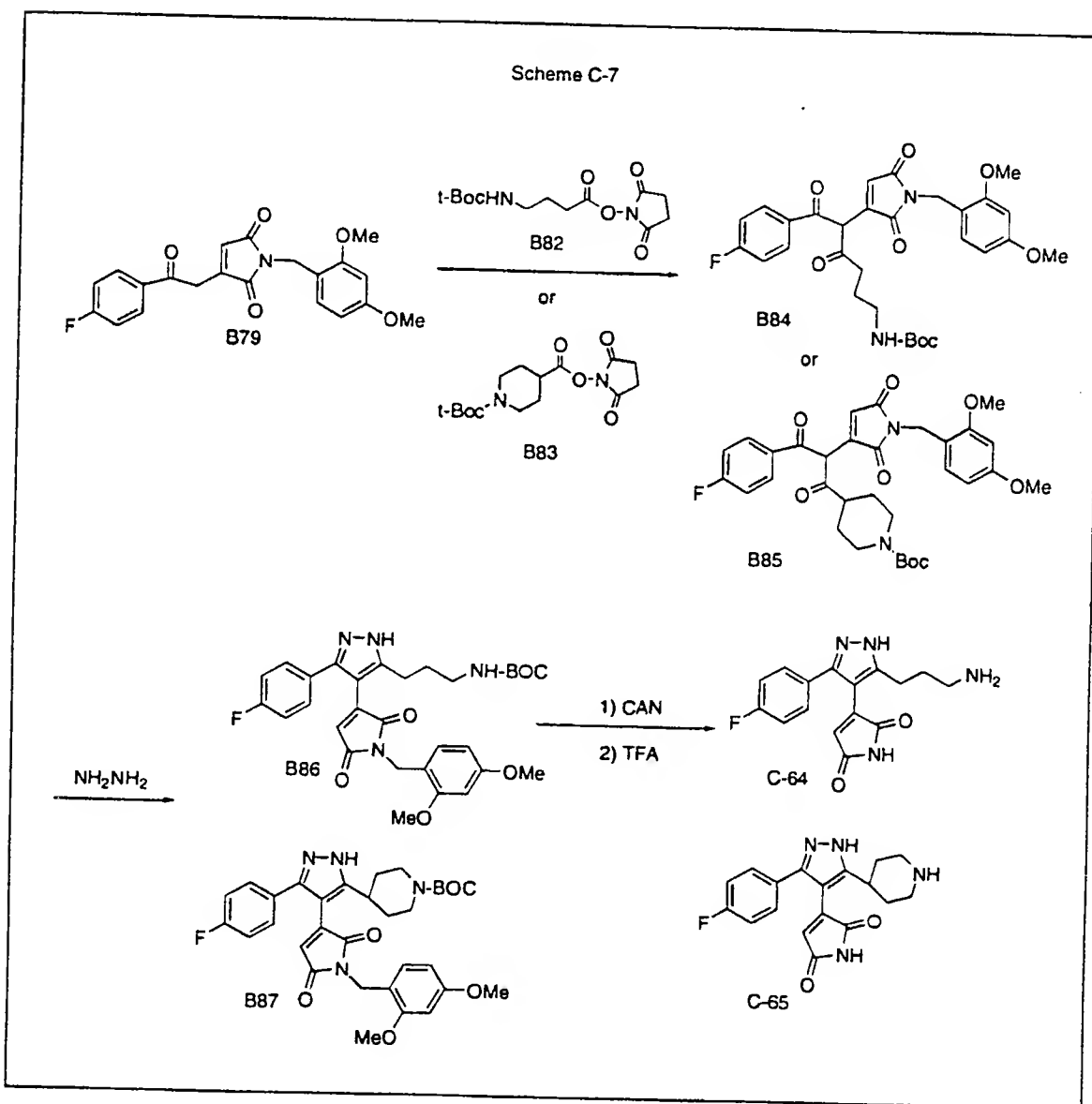
$\text{Pd}_2(\text{dba})_3$  and sodium *t*-butoxide to form the fluoroacetophenone substituted maleimide **B79**. The **B79** is treated with *tert*-butoxybis(dimethylamino)methane to yield the  $\alpha$ -ketoenamine **B80**. The  $\alpha$ -ketoenamine **B80** is condensed with hydrazine to form the maleimide pyrazole skeleton **B81**. The 2, 4-dimethoxybenzyl group protecting group is optionally removed with ceric ammonium nitrate (CAN) to give compound **C-63**.



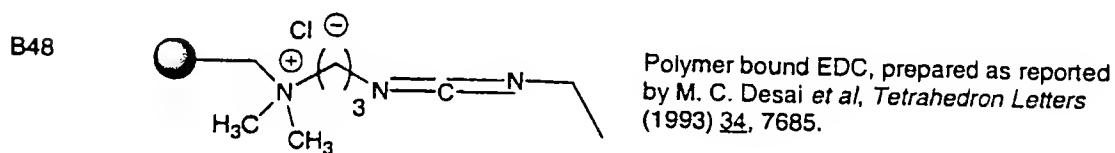
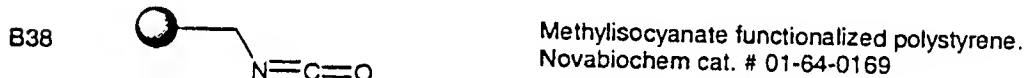
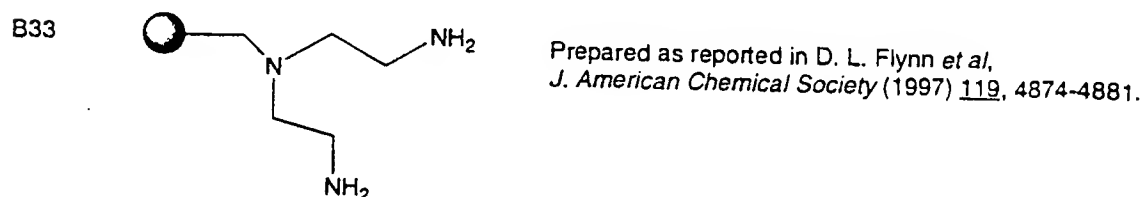
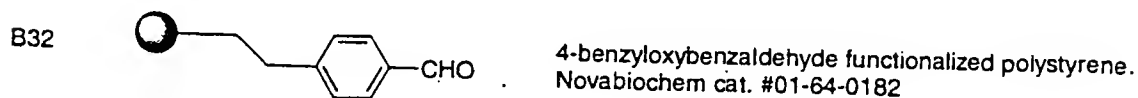
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Scheme C-7 illustrates the synthesis of maleimide-containing scaffolds **C-64** and **C-65**. These scaffolds **C-49** and **C-50** are synthesized according to the general methods

illustrated in Scheme C-5 and exemplified with the utilization of N-hydroxysuccinimides **B82** and **B83** to afford the maleimide-containing pyrazoles **B86** and **B87**, respectively. Optional removal of the 2,4-dimethoxybenzyl groups with CAN and subsequent removal of the Boc-protecting groups with trifluoroacetic acid (TFA) affords the scaffolds **C-64** and **C-65**.



The various functionalized resins and sequestration-enabling-reagents utilized to prepare and purify parallel reaction mixtures are more fully described below, including their commercial source or literature reference to their preparation.



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Experimental procedure for the parallel synthesis of a series of amides, carbamates, ureas and sulfonamides B-0001 through B-0048 from scaffold C-1.

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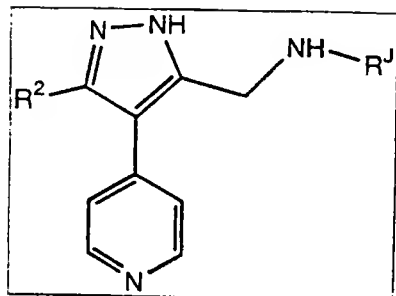
#### Examples B-0001 through B-0048

To each reaction vessel (polypropylene syringe tubes fitted with a porous frit, closed at the bottom) of a parallel reaction apparatus was added 200 uL of dimethylformamide. A stock solution of the scaffold amine C-1 in dimethylformamide (0.1 M, 500 uL) was added to each reaction vessel followed by the addition of a stock solution of N-methylmorpholine in dimethylformamide (1.0 M., 200 uL). A stock solution of each of the electrophiles was then added to the appropriate reaction vessels: a) 500 uL of a 0.2 M solution of the acid chlorides in dichloroethane or b) 500 uL of a 0.2 M solution of the chloroformates in dichloroethane or c) 313 uL of a 0.2 M solution of the isocyanates in dichloroethane or d) 375 uL of a 0.2 M solution of the sulfonyl chlorides in dichloroethane. The parallel reaction apparatus was then orbitally shaken (Labline Benchtop orbital shaker) at 200 RPM at ambient

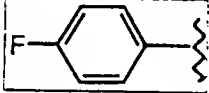
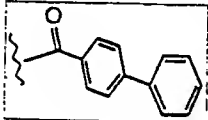
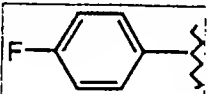
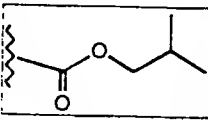
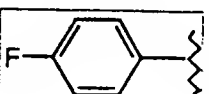
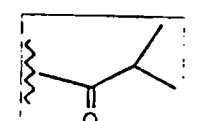
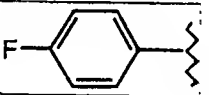
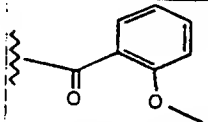
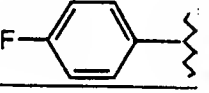
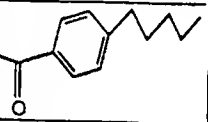
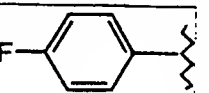
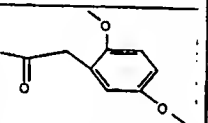
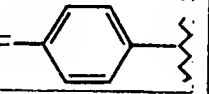
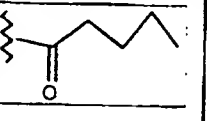
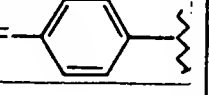
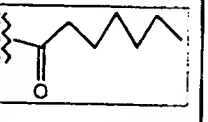
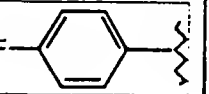
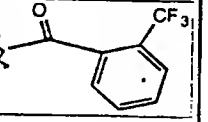
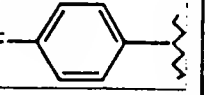
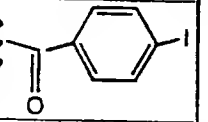
temperature (23-30 °C) for a period of 2-3 h, under a gentle flow of nitrogen. At this time each reaction vessel was treated with approximately 250 mg of polyamine resin **B33** (4.0 meq N/g resin) and approximately 100 mg of polyaldehyde resin **B32** (2.9 mmol/g resin). Each reaction vessel was diluted with 1 mL dimethylformamide and 1 mL dichloroethane and the orbital shaking was continued at 200 RPM for a period of 14-20 h at ambient temperature. Each reaction vessel was then opened and the desired solution phase products separated from the insoluble quenched byproducts by filtration and collected in individual conical vials. Each vessel was rinsed twice with dichloroethane (1 mL) and the rinsings were also collected. The solutions obtained were then evaporated to dryness in a Savant apparatus (an ultracentrifuge equipped with high vacuum, scalable temperature settings and a solvent trap to condense the volatile solvent vapors). The resulting amide, carbamate, urea and sulfonamide products were then weighed and characterized. The yields and analytical data for the products obtained using this method are shown below.

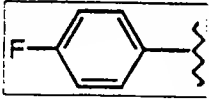
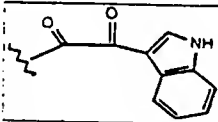
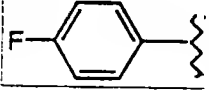
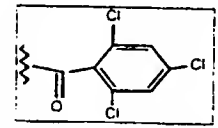
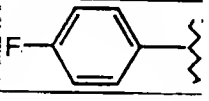
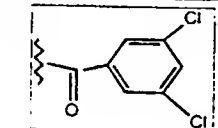
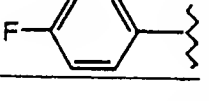
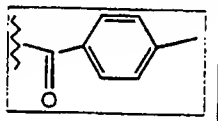
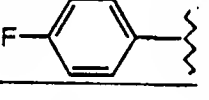
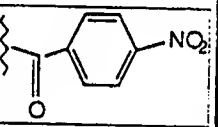
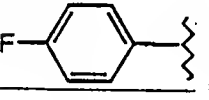
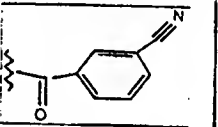
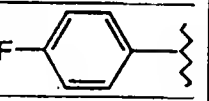
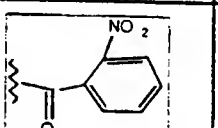
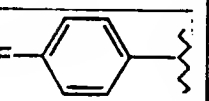
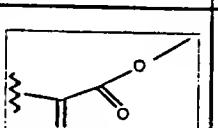
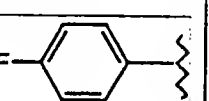
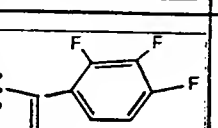
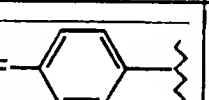
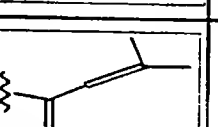
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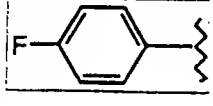
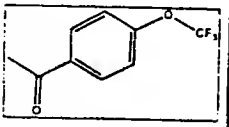
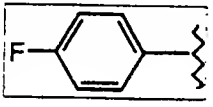
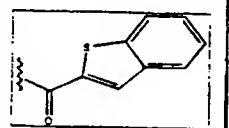
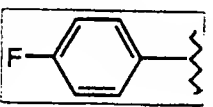
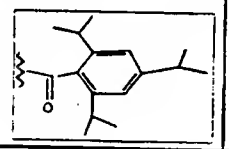
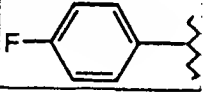
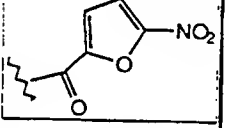
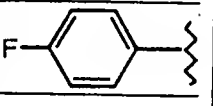
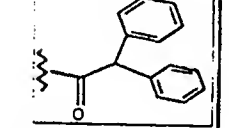
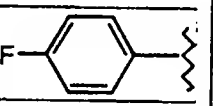
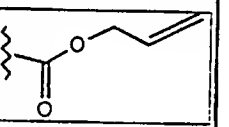
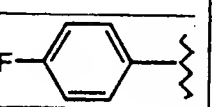
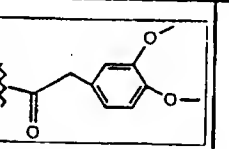
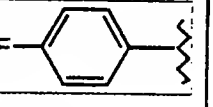
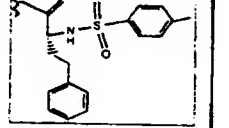
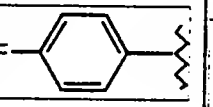
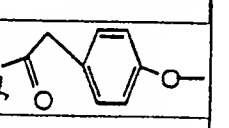
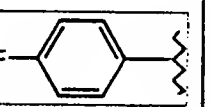
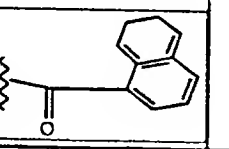
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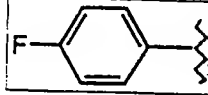
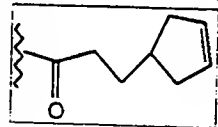
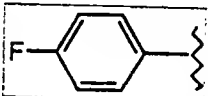
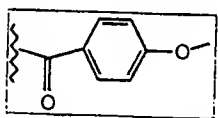
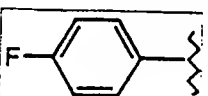
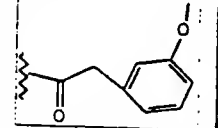
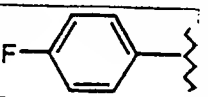
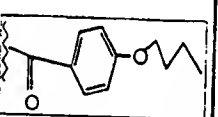
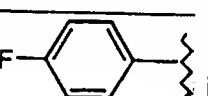
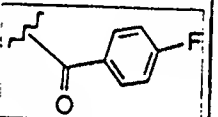
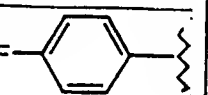
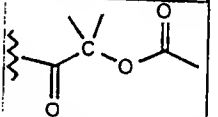
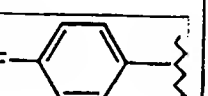
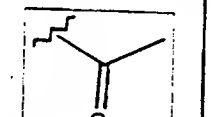
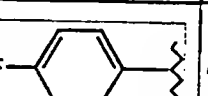
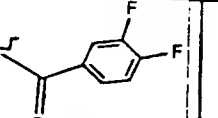
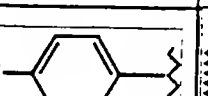
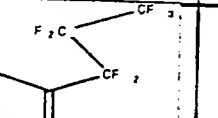
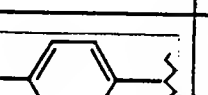
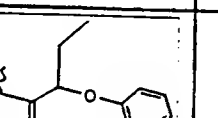


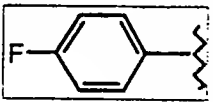
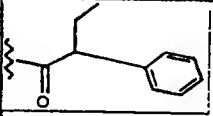
Example#	R²	R¹	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0001			85	397	398
B-0002			94	412	413
B-0003			91	340	341
B-0004			79	368	369
B-0005			92	498	499
B-0006			92	416	417
B-0007			86	450	451

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0008			86	448	449
B-0009			83	368	369
B-0010			86	338	339
B-0011			92	402	403
B-0012			74	442	443
B-0013			91	446	447
B-0014			84	352	353
B-0015			94	380	381
B-0016			89	440	441
B-0017			83	498	499

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0018			24	439	440
B-0019			89	474	475
B-0020			90	440	441
B-0021			85	386	387
B-0022			35	417	418
B-0023			94	397	398
B-0024			87	417	418
B-0025			5	354	-
B-0026			87	426	427
B-0027			89	350	351

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0028			92	456	457
B-0029			89	428	429
B-0030			37	498	499
B-0031			18	407	408
B-0032			86	462	463
B-0033			3	352	-
B-0034			92	446	447
B-0035			28	569	570
B-0036			93	416	417
B-0037			91	422	423

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0038			84	390	393
B-0039			87	402	403
B-0040			92	416	417
B-0041			75	444	445
B-0042			54	390	391
B-0043			80	396	397
B-0044			81	310	311
B-0045			91	408	409
B-0046			25	464	465
B-0047			88	430	431

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0048			95	414	415

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By analogy to the procedure identified above for the preparation of Examples B0001-B0048, the following examples B-0049 through B-1573 were prepared.

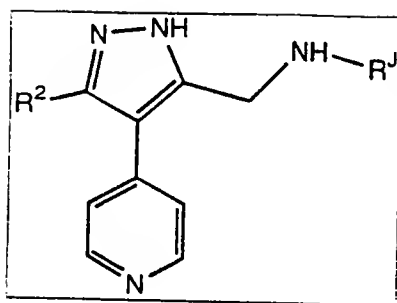
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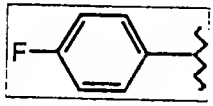
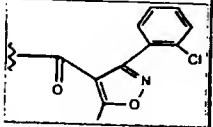
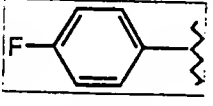
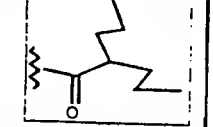
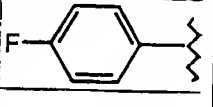
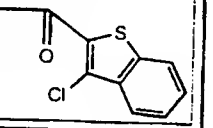
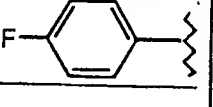
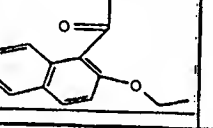
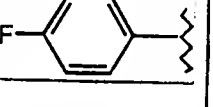
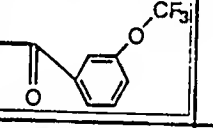
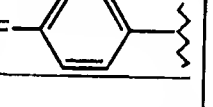
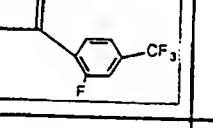
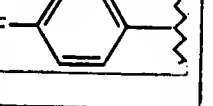
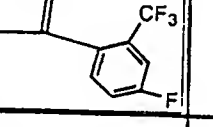
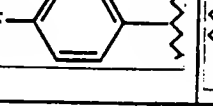
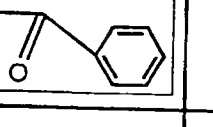
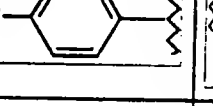

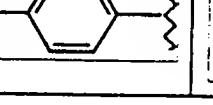
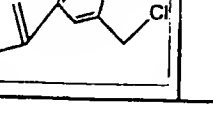
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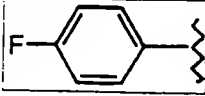
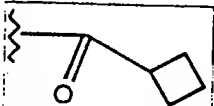
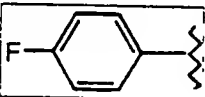
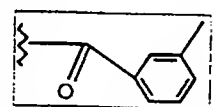
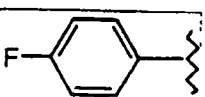
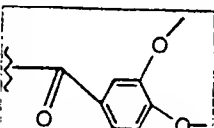
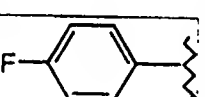
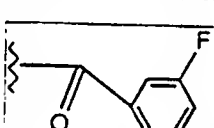
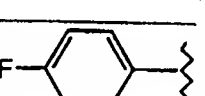
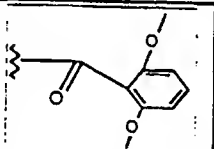
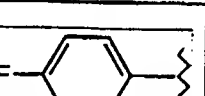
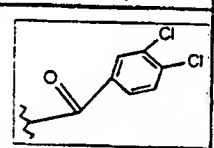

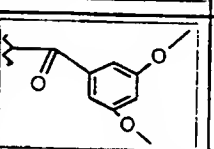
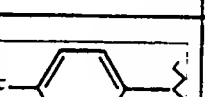
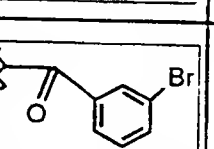

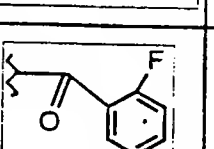
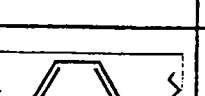
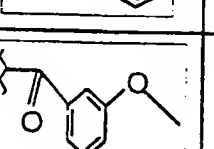
Example#

	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0049			85	414	415
B-0050			9	458	459
B-0051			91	426	427
B-0052			79	407	408
B-0053			92	407	408
B-0054			92	363	364
B-0055			86	505	506

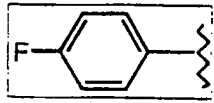
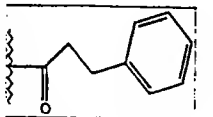
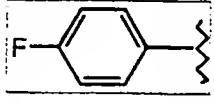
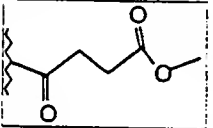
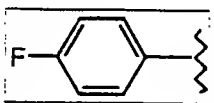
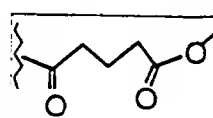
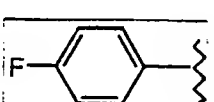
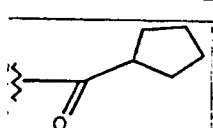
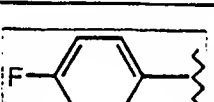
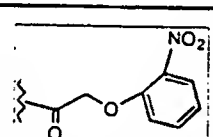
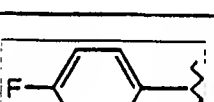
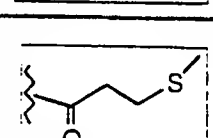

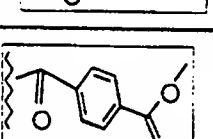

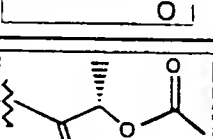

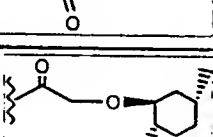

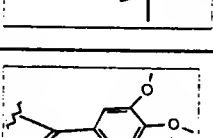
Example#

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0056			86	487	488
B-0057			83	394	395
B-0058			86	462	463
B-0059			92	466	467
B-0060			74	456	457
B-0061			35	458	459
B-0062			94	458	459
B-0063			87	372	373
B-0064			5	394	395
B-0065			87	420	395


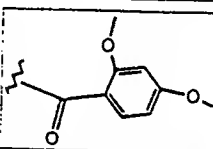
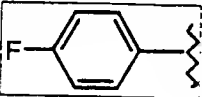
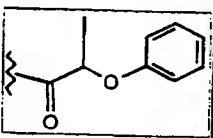
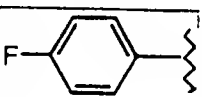
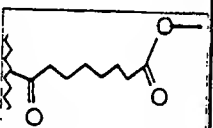
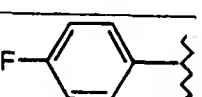
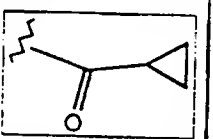
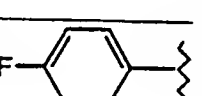
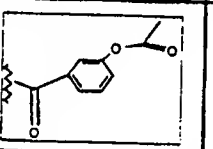
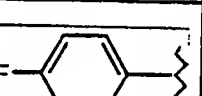
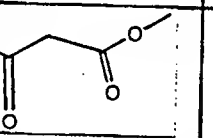
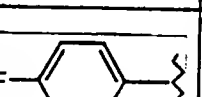
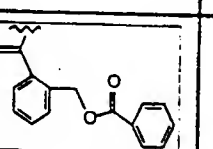
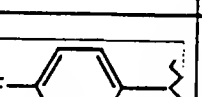
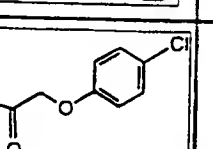
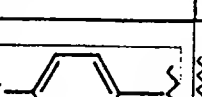
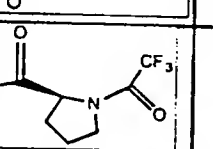
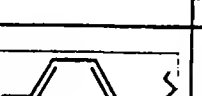
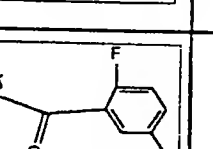
Example#

	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0066			89	350	351
B-0067			92	386	387
B-0068			89	432	433
B-0069			37	390	391
B-0070			18	432	433
B-0071			86	440	441
B-0072			3	432	433
B-0073			92	450	451
B-0074			28	390	391
B-0075			93	402	403

Example#

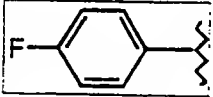
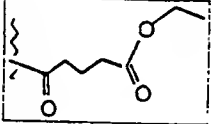
	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0076			91	400	401
B-0077			84	382	383
B-0078			87	396	397
B-0079			92	364	365
B-0080			75	447	448
B-0081			54	370	371
B-0082			80	430	431
B-0083			81	382	383
B-0084			91	464	465
B-0085			25	462	463

Example#

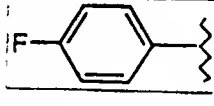
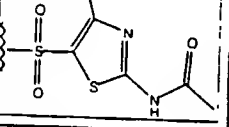
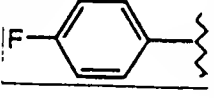
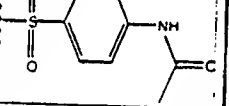
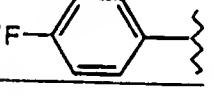
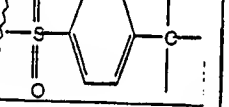
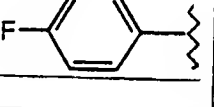

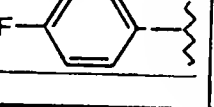
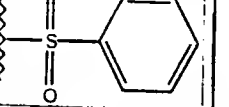
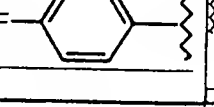
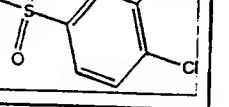
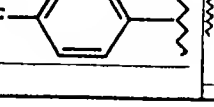
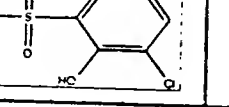
	R <sup>2</sup>	R <sup>J</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0086			88	432	433
B-0087			95	416	417
B-0088				438	439
B-0089				336	337
B-0090				444	445
B-0091				368	369
B-0092				506	507
B-0093				436	437
B-0094				461	462
B-0095				408	409

591

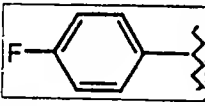
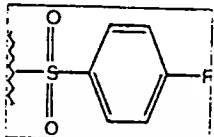
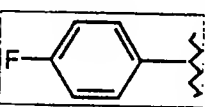
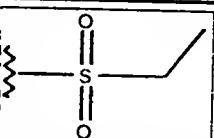
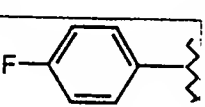
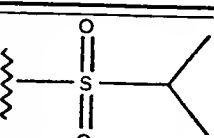
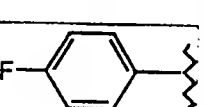
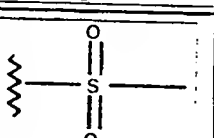
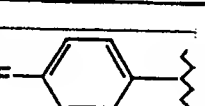
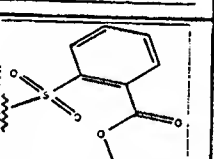
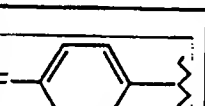
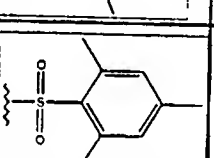
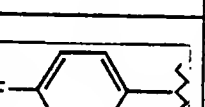
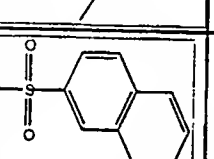
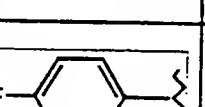
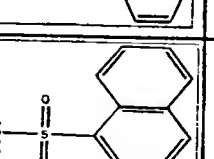
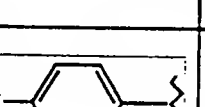
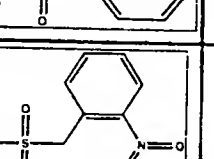

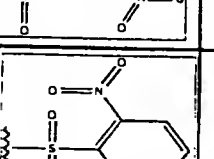
Example#

	R <sup>2</sup>	R <sup>J</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0096				410	411

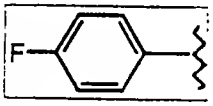
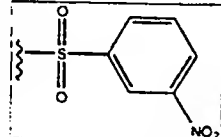
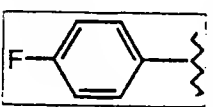
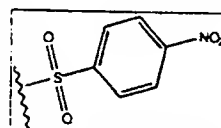
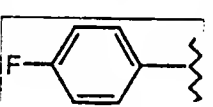
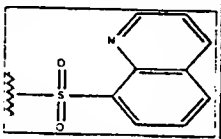
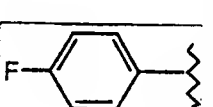
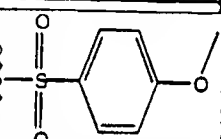
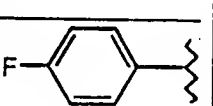
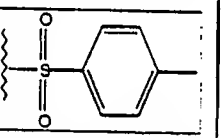
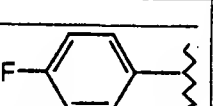
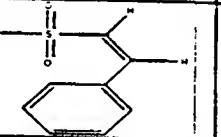
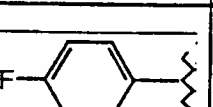
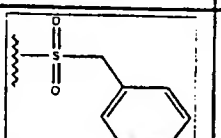
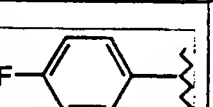
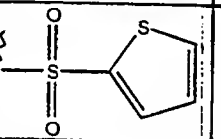
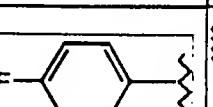
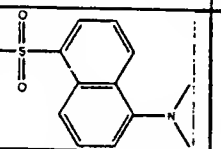
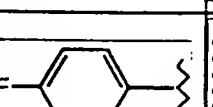
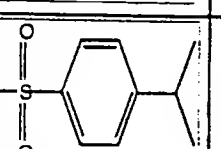
Example#

	R <sup>2</sup>	R <sup>J</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0097			14	486	487
B-0098			8	465	-
B-0099			75	464	465
B-0100			72	388	389
B-0101			23	408	409
B-0102			37	487	488
B-0103			11	492	493

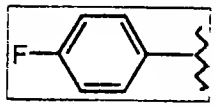
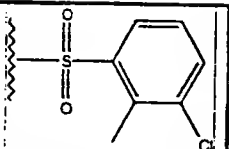
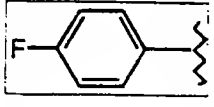
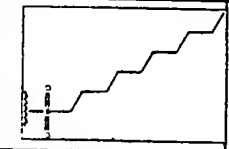
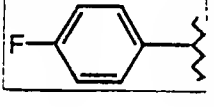
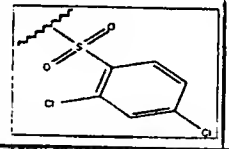
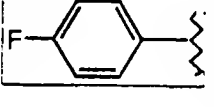
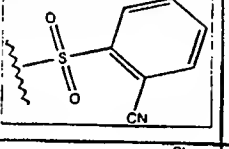
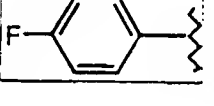
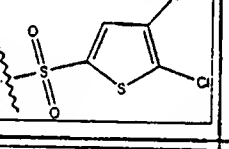
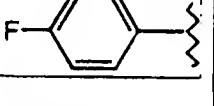
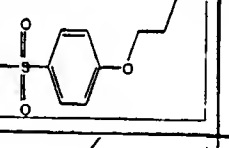
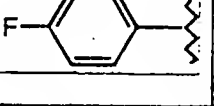
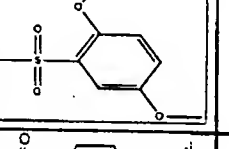
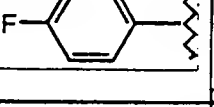
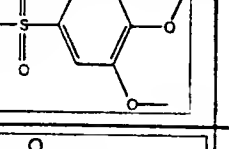
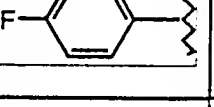
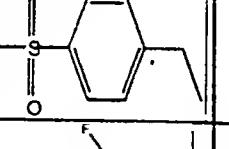
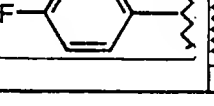
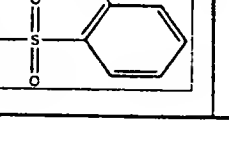
Example#

	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0104			59	426	427
B-0105			79	360	361
B-0106			56	374	375
B-0107			33	346	347
B-0108			12	466	467
B-0109			65	450	451
B-0110			55	458	459
B-0111			41	458	459
B-0112			19	467	468
B-0113			78	453	454

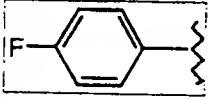
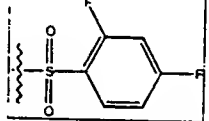
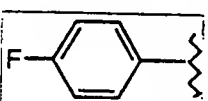
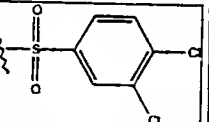
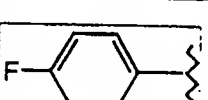
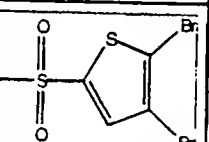
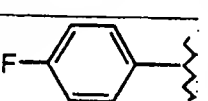
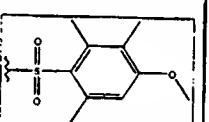
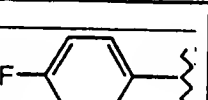
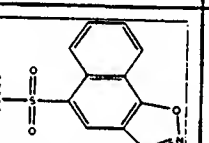
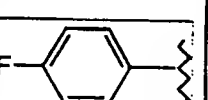
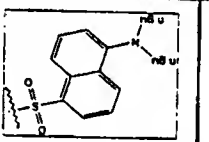
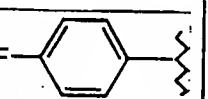
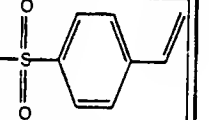
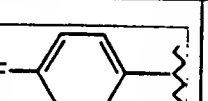
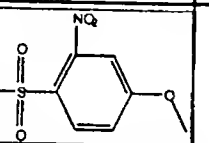
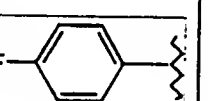
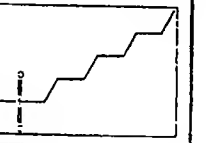
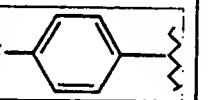
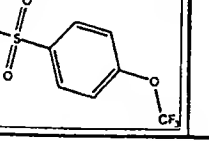
Example#

	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0114			14	453	454
B-0115			33	453	
B-0116			11	459	487
B-0117			77	438	439
B-0118			52	422	423
B-0119			82	434	435
B-0120			49	422	423
B-0121			64	414	415
B-0122			87	501	502
B-0123			100	450	451

Example#

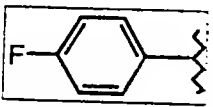
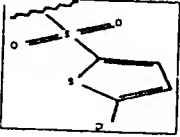
	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0124			87	456	457
B-0125			45	472	473
B-0126			100	476	477
B-0127			100	433	434
B-0128			100	482	-
B-0129			96	480	481
B-0130			93	468	469
B-0131			90	468	469
B-0132			78	436	437
B-0133			76	426	427

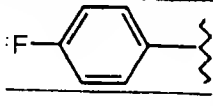
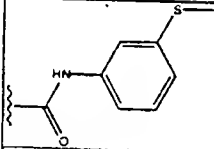
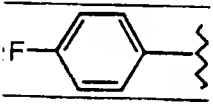
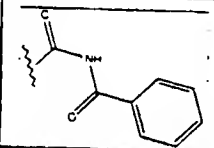
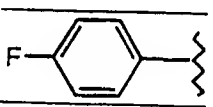
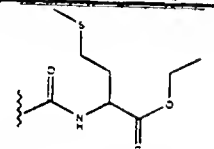
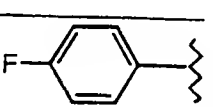
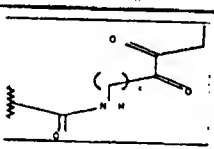
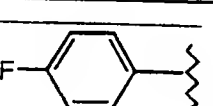
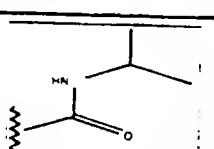
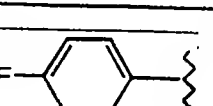
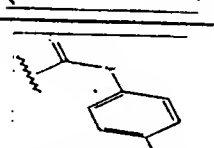
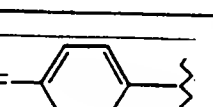
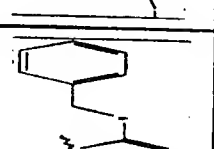
Example#

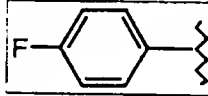
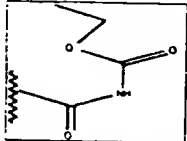
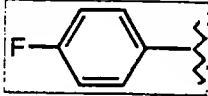
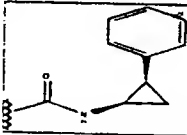
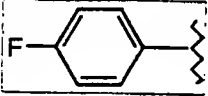
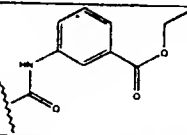
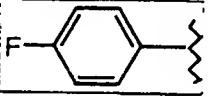
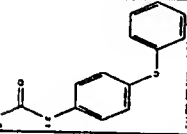
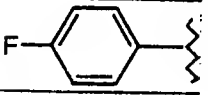
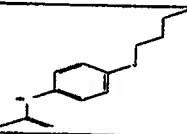
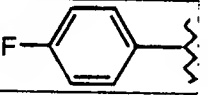
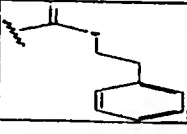
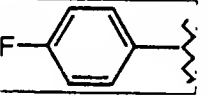
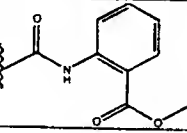
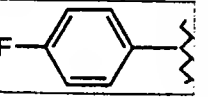
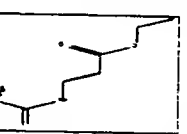
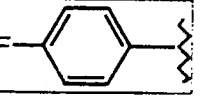
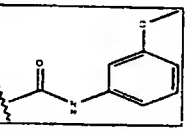
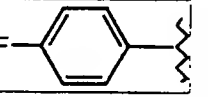
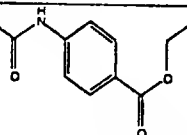
	R <sup>2</sup>	R <sup>3</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0134			87	444	445
B-0135			67	476	477
B-0136			100	570	-
B-0137			35	480	481
B-0138			60	500	-
B-0139			73	585	586
B-0140			62	434	459
B-0141			100	483	484
B-0142			90	444	445
B-0143			61	492	493

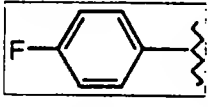
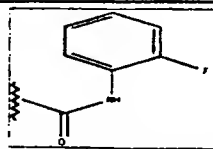
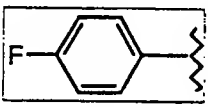
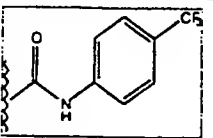
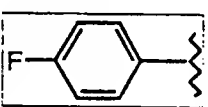
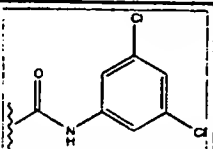
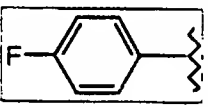
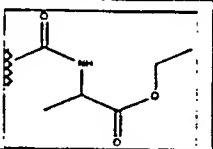
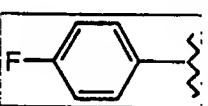
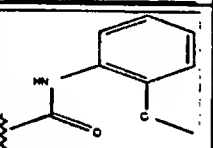
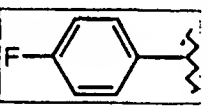
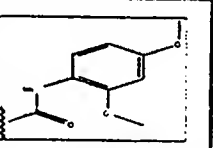
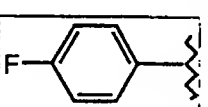
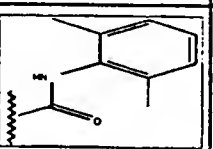
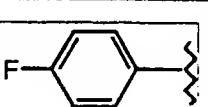
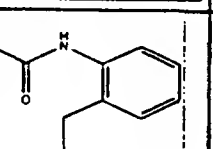
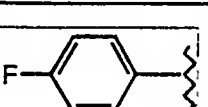
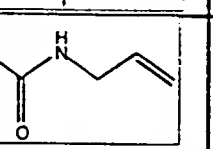
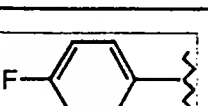
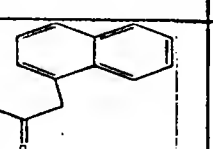
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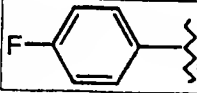
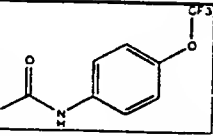
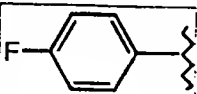
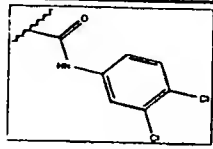
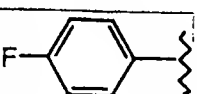
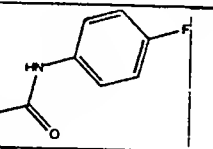
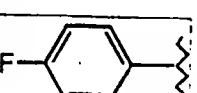
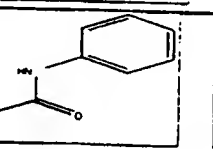
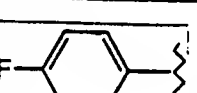
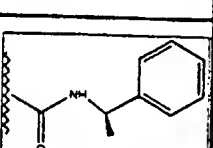
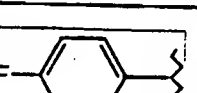
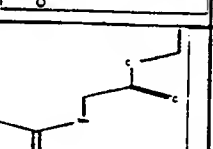
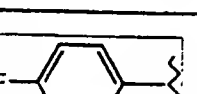
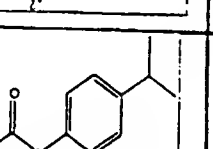
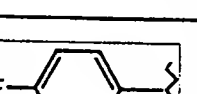
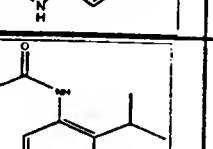

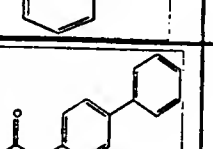

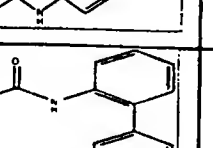
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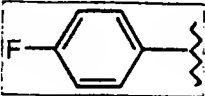
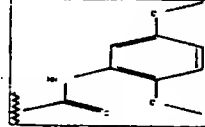
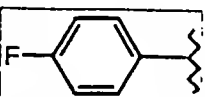
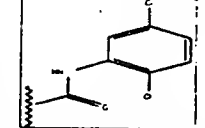
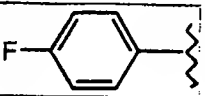
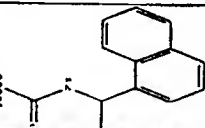
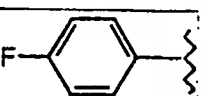
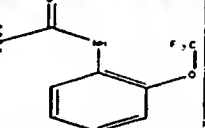
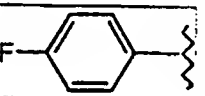
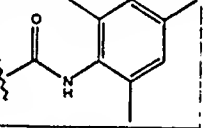
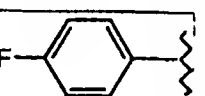
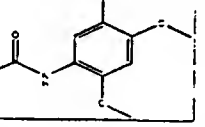
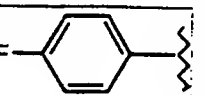
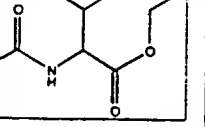
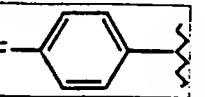
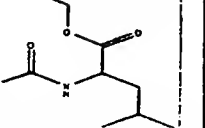
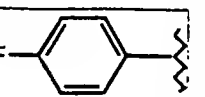
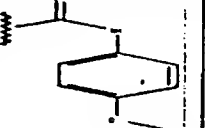
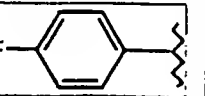
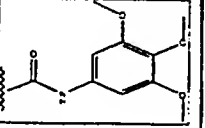
	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0144			49	448	449

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0145			48	433	434
B-0146			32	415	416
B-0147			67	471	472
B-0148			79	465	-
B-0149			65	353	354
B-0150			53	465	466
B-0151			68	401	402

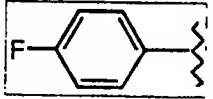
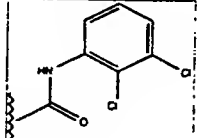
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0152			39	383	-
B-0153			96	427	428
B-0154			44	459	460
B-0155			74	479	480
B-0156			44	459	460
B-0157			72	415	416
B-0158			96	445	446
B-0159			97	411	412
B-0160			49	417	418
B-0161			93	459	460

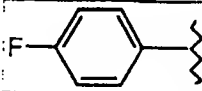
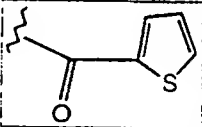
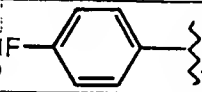
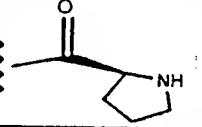
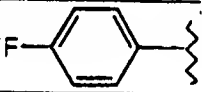
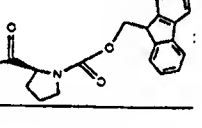
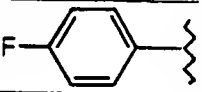
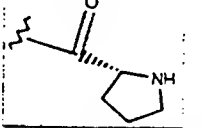
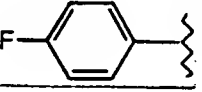
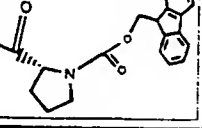
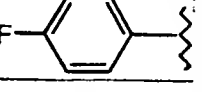
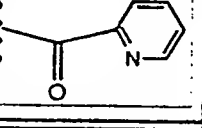
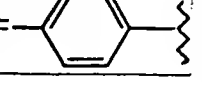
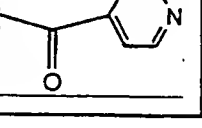
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0162			91	405	406
B-0163			94	455	456
B-0164			84	455	456
B-0165			52	411	412
B-0166			72	417	418
B-0167			66	447	448
B-0168			27	415	416
B-0169			91	415	416
B-0170			8	351	352
B-0171			10	437	438

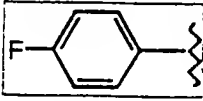
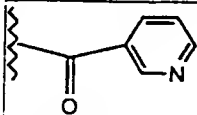
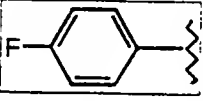
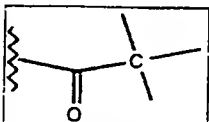
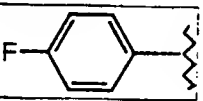
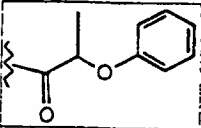
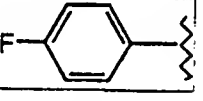
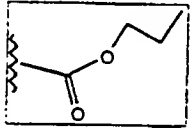
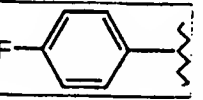
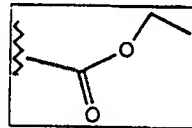
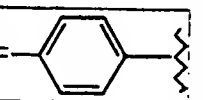
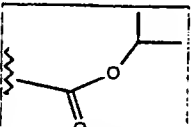
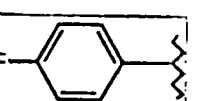
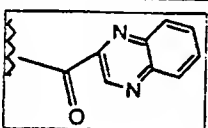

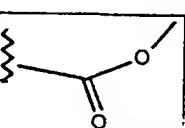
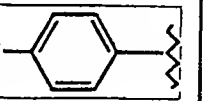
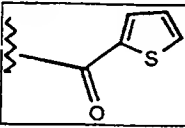
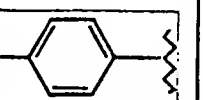
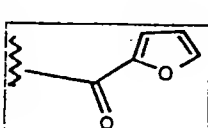
Example#	R <sup>2</sup>	R <sup>J</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0172			62	471	472
B-0173			40	455	456
B-0174			92	405	406
B-0175			96	387	388
B-0176			25	415	416
B-0177			100	397	398
B-0178			34	429	430
B-0179			72	429	430
B-0180			91	463	464
B-0181			100	463	464

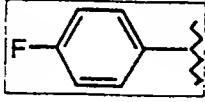
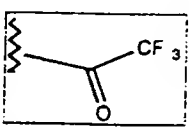
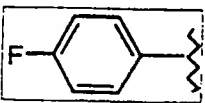
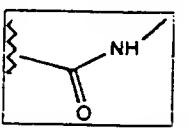
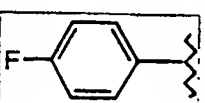
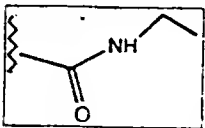
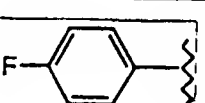
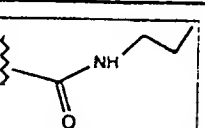
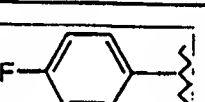
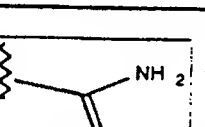
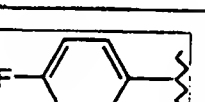
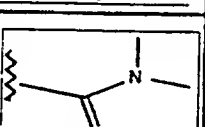
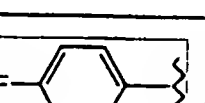
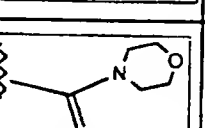
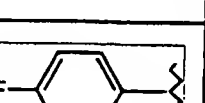
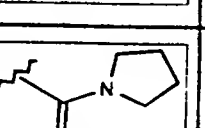
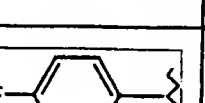
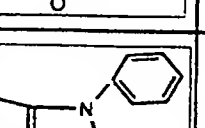

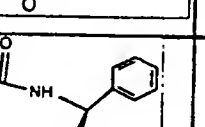
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0182			50	447	448
B-0183			22	455	456
B-0184			63	465	466
B-0185			65	471	472
B-0186			42	429	430
B-0187			62	481	482
B-0188			98	439	440
B-0189			21	453	454
B-0190			57	417	418
B-0191			24	477	478

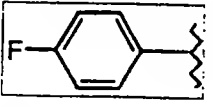
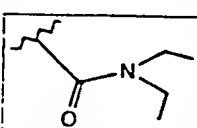
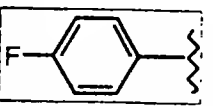
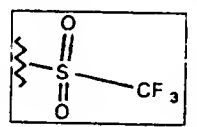
603

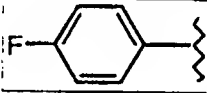
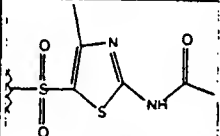
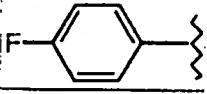
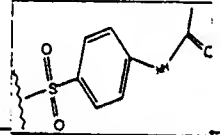
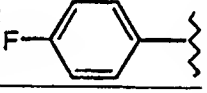
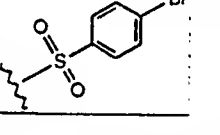
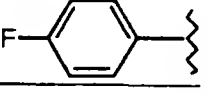
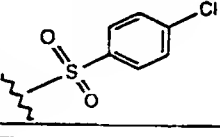
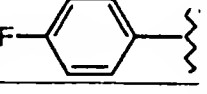
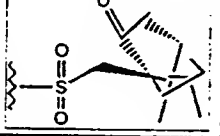
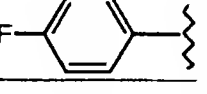
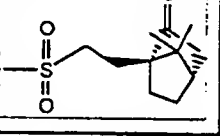
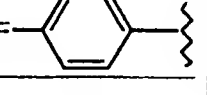
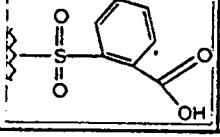
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0192			35	455	456

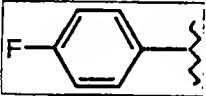
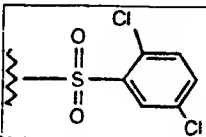
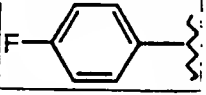
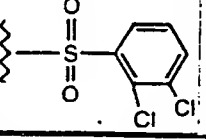
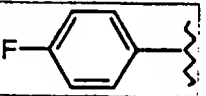
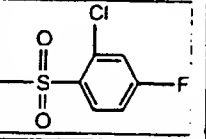
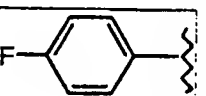
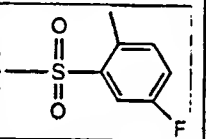
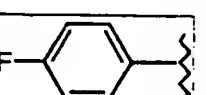
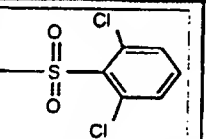
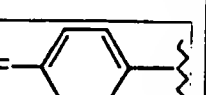
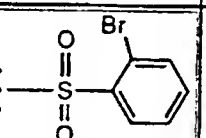
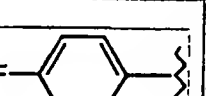
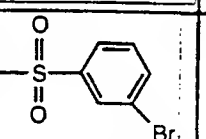
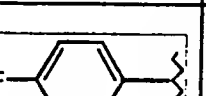
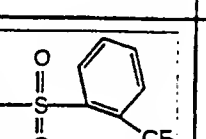
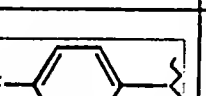
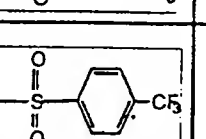
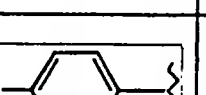
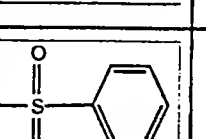
Example#	R <sup>2</sup>	R <sup>3</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0193			42	378	379
B0194			65	365	366
B-0195			93	587	588
B-0196			82	365	366
B-0197			100	587	588
B-0198			86	373	374
B-0199			81	373	374


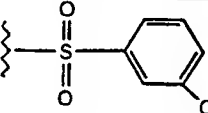
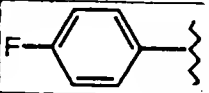
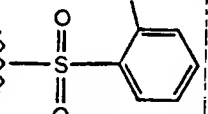
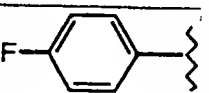
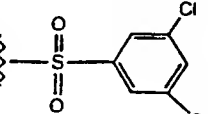
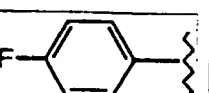
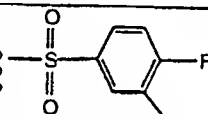
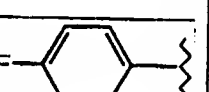
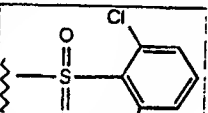
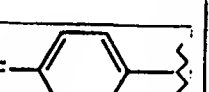
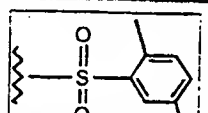
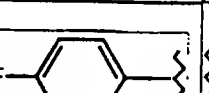
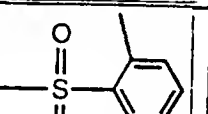
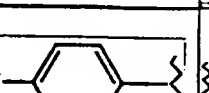
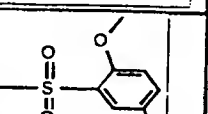
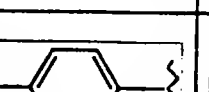
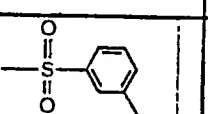

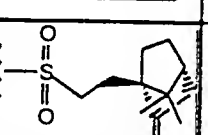
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0200			78	373	374
B-0201			95	352	353
B-0202			100	416	417
B-0203			69	354	355
B-0204			93	340	341
B-0205			94	354	355
B-0206			79	424	425
B-0207			82	326	327
B-0208			88	378	379
B-0209			83	362	363

Example#	R <sup>2</sup>	R <sup>3</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0210			100	364	365
B-0211			60	325	326
B-0212			79	339	340
B-0213			71	353	354
B-0214			77	311	312
B-0215			24	353	354
B-0216				339	340
B-0217				381	382
B-0218				365	366
B-0219				401	402

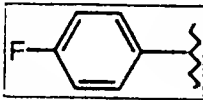
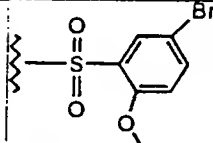
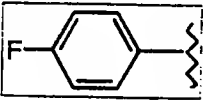
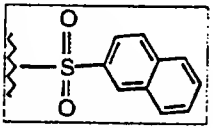
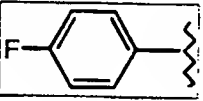
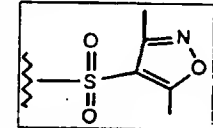
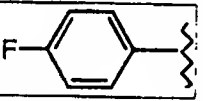
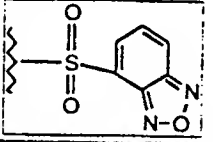
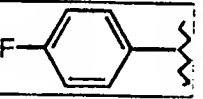
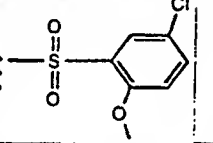
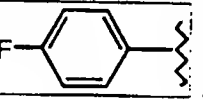
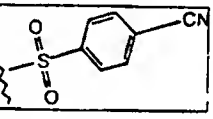

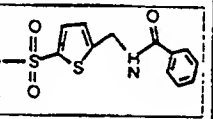

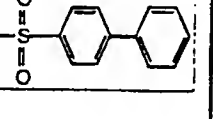
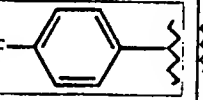
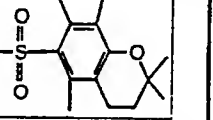
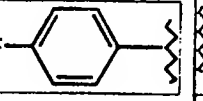
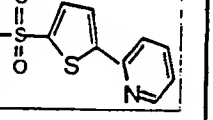
Example#	R <sup>2</sup>	R <sup>J</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0220				415	416
B-0221				367	368

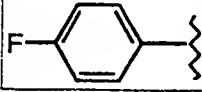
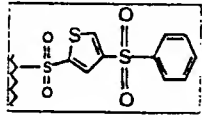
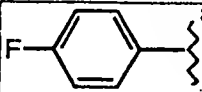
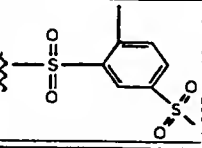
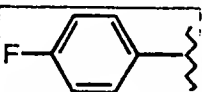
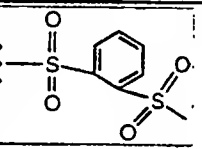
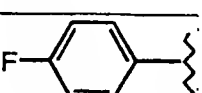
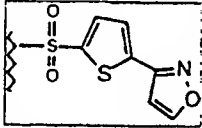
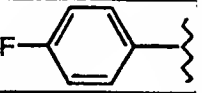
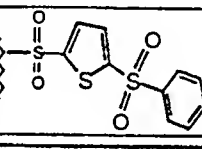
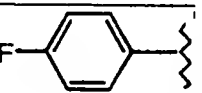
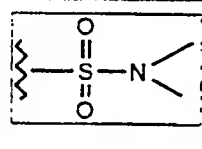
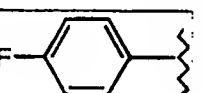
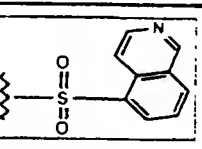
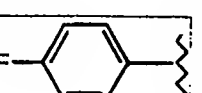
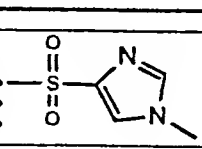
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0222			96	486	487
B-0223			100	465	466
B-0224			75	486	509a
B-0225			100	442	443
B-0226			88	482	483
B-0227			73	482	483
B-0228			37	452	-

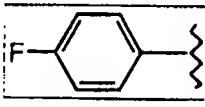
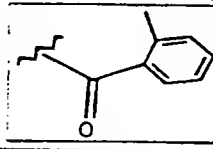
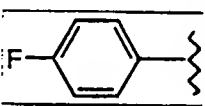
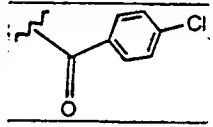
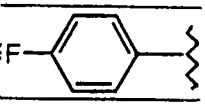
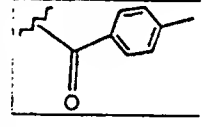
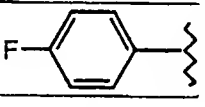
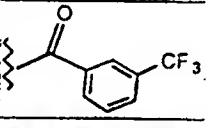
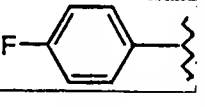
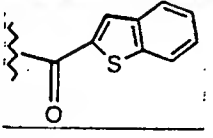
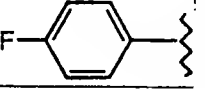
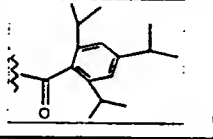
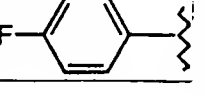
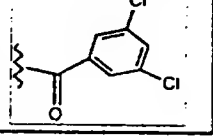
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0229			100	476	477
B-0230			94	476	477
B-0231			100	460	461
B-0232			90	440	441
B-0233			99	476	477
B-0234			100	486	487,489
B-0235			89	486	487,489
B-0236			100	476	477
B-0237			100	476	477
B-0238			92	438	-

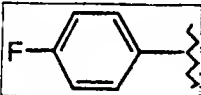
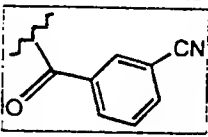
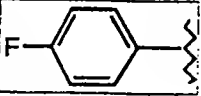
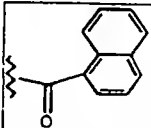
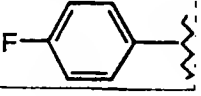
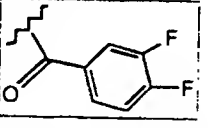
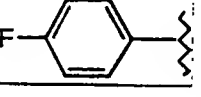
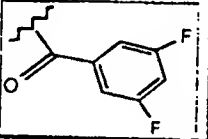
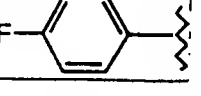
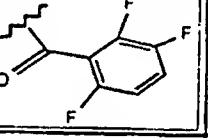
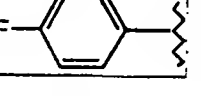
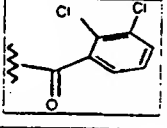
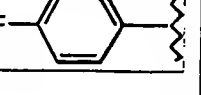
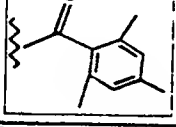
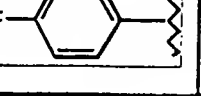
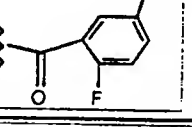
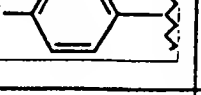
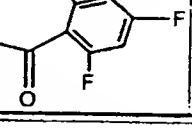
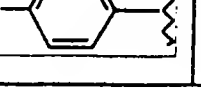
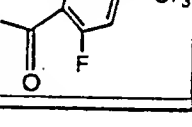
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0239			100	442	443
B-0240			100	442	443
B-0241			100	476	477
B-0242			100	460	461
B-0243			87	456	457
B-0244			100	436	437
B-0245			100	422	423
B-0246			100	452	453
B-0247			100	476	477
B-0248			73	468	-


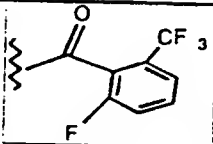
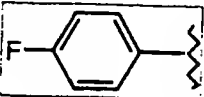
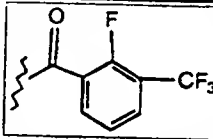
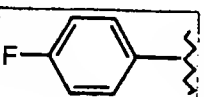
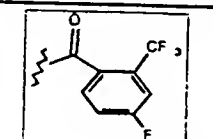
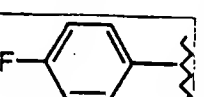
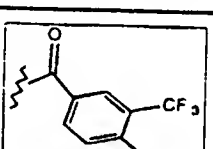
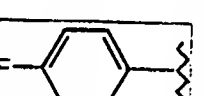
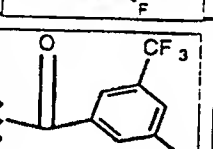
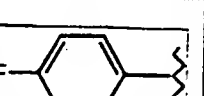
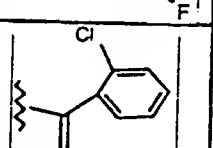
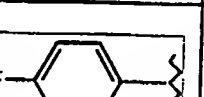
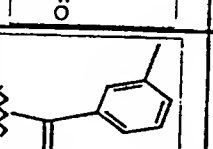
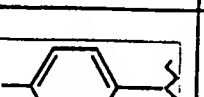
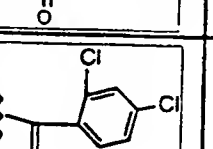
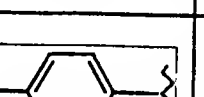
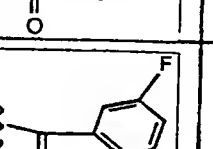

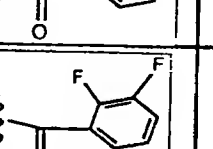
R<sup>1</sup>

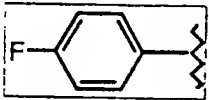
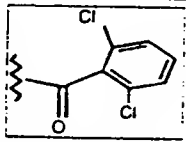
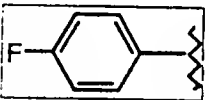
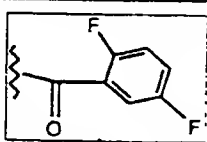
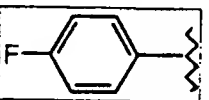
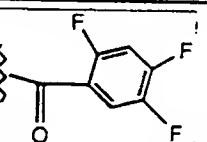
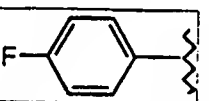
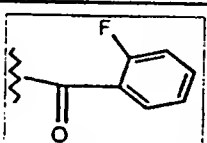
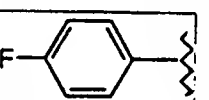
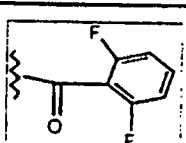
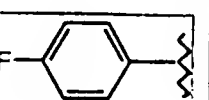
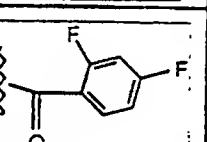
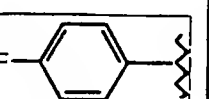
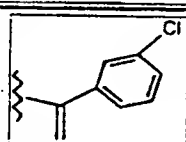
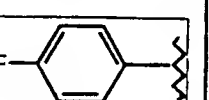
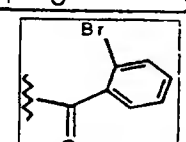
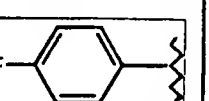
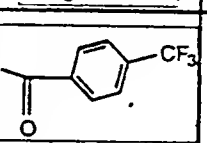
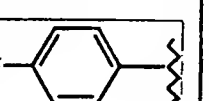
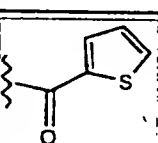
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0249			100	516	517,519
B-0250			72	458	-
B-0251			100	427	428
B-0252			100	450	451
B-0253			100	472	473
B-0254			100	433	434
B-0255			84	547	548
B-0256			100	484	507a
B-0257			85	534	535
B-0258			100	491	492

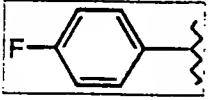
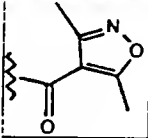
Example#	R <sup>2</sup>	R <sup>J</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0259			100	554	555
B-0260			91	500	501
B-0261			100	486	487
B-0262			100	481	482
B-0263			100	554	555
B-0264			75	375	376
B-0265			71	459	460
B-0266			100	412	413

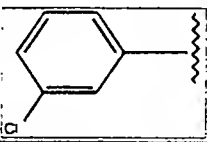
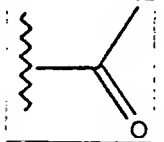
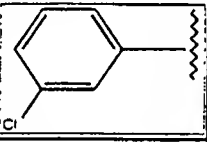
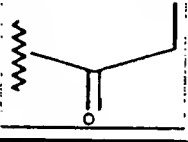
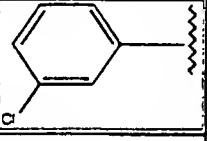
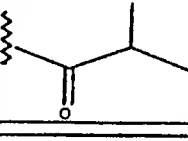
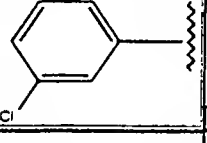
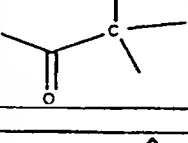
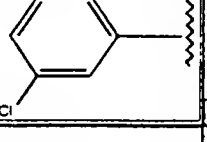
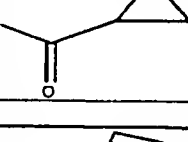
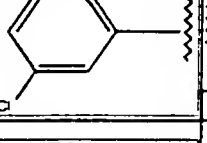
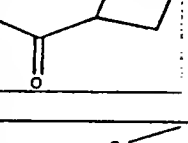
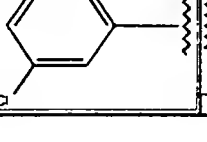
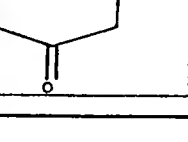
Example#	R <sup>2</sup>	R <sup>4</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0267			100	386	387
B-0268			89	406	407
B-0269			84	386	387
B-0270			92	440	441
B-0271			98	428	429
B-0272			57	498	499
B-0273			100	440	441

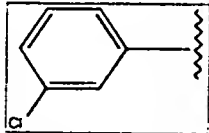
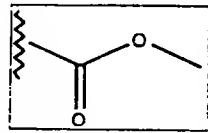
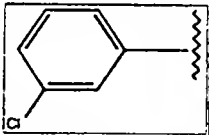
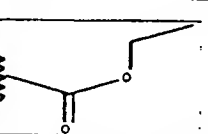
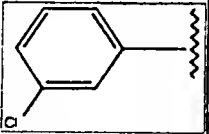
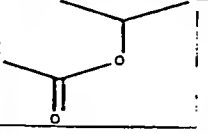
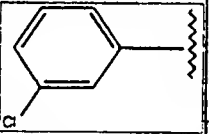
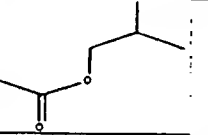
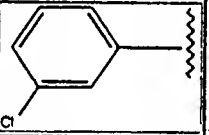
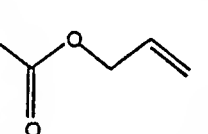
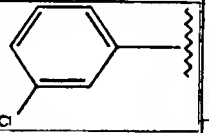
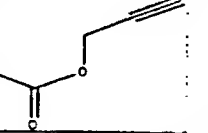
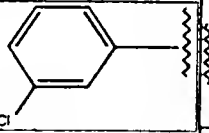
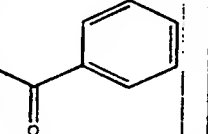
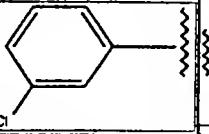
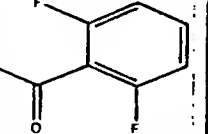
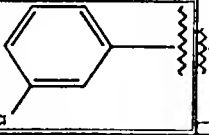
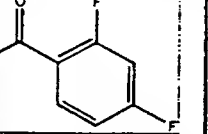
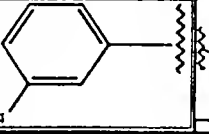
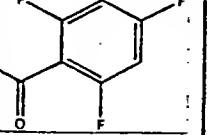
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0274			94	397	398
B-0275			90	422	423
B-0276			100	408	409
B-0277			88	408	409
B-0278			100	426	427
B-0279			54	440	441
B-0280			79	414	415
B-0281			82	458	459
B-0282			89	426	427
B-0283			90	458	459

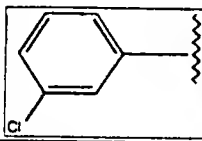
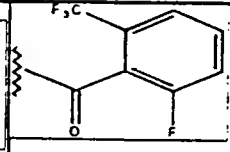
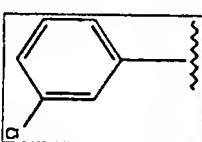
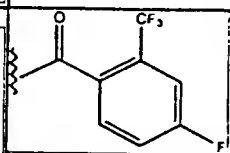
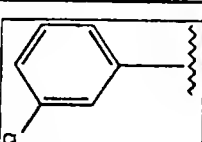
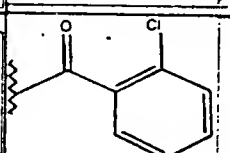
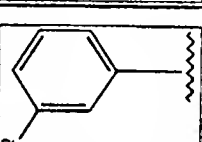
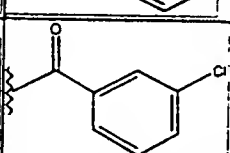
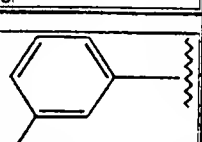
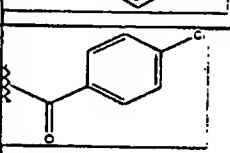
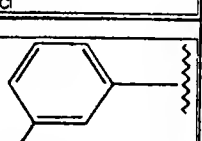
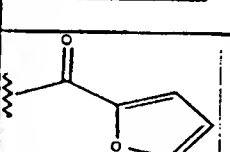
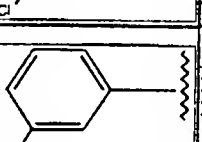
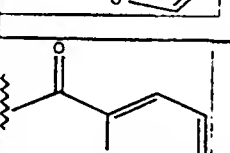
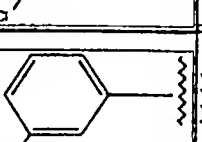
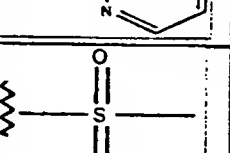
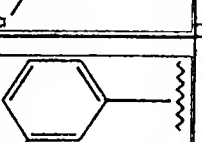
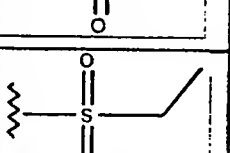
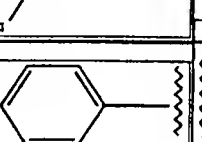
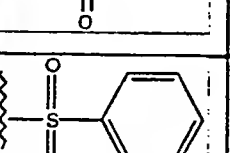
Example#	R <sup>2</sup>	R <sup>J</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0284			100	458	459
B-0285			94	458	459
B-0286			100	458	459
B-0287			96	458	459
B-0288			100	458	459
B-0289			96	406	407
B-0290			96	386	387
B-0291			95	440	441
B-0292			94	390	391
B-0293			100	408	409

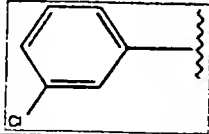
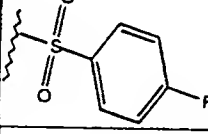
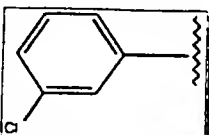
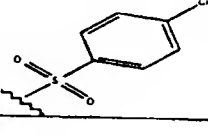
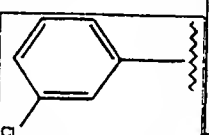
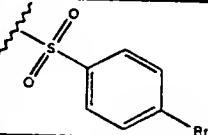
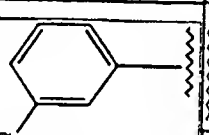
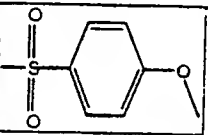
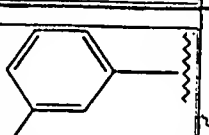
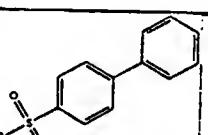
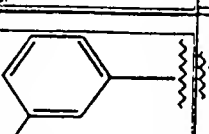
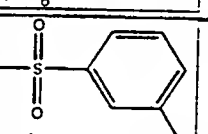
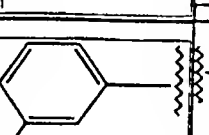
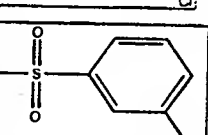
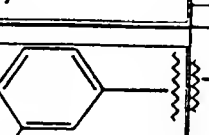
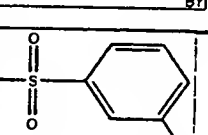
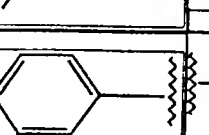
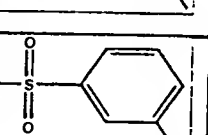
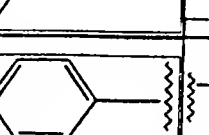
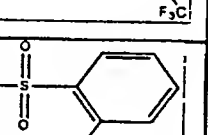
Example#	R <sup>2</sup>	R <sup>J</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0294			100	440	441
B-0295			91	408	409
B-0296			96	426	427
B-0297			88	390	391
B-0298			95	408	409
B-0299			90	408	409
B-0300			95	406	407
B-0301			99	450	451,453
B-0302			94	440	441
B-0303			100	378	379

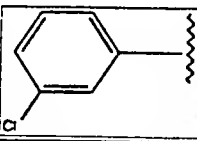
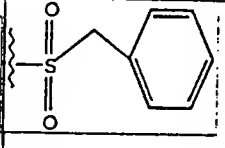
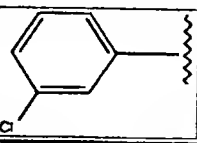
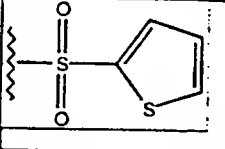
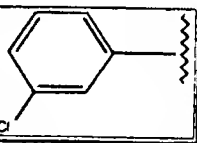
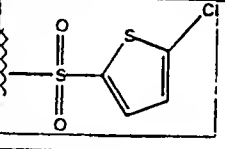
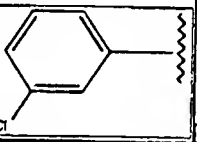
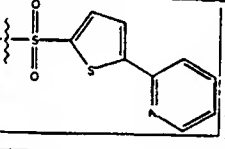
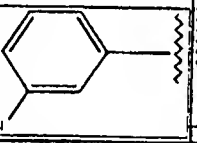
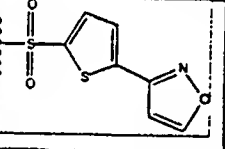
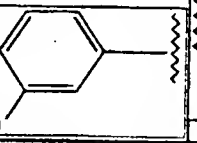
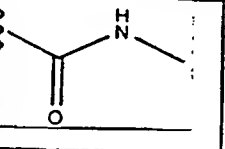
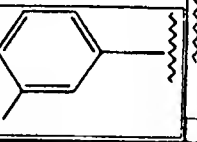
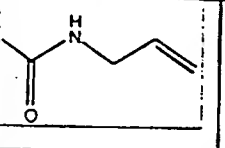
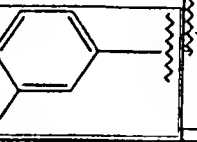
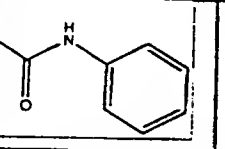
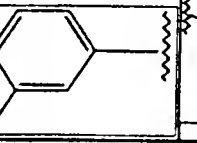
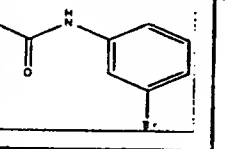
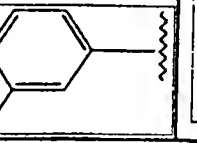
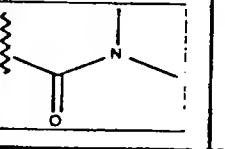
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0304			100	391	392

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0305			70	326	327
B-0306			59	340	341
B-0307			59	354	355
B-0308			60	368	369
B-0309			61	352	353
B-0310			61	366	367
B-0311			65	356	357

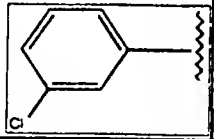
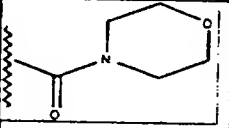
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0312			75	342	343
B-0313			68	356	357
B-0314			31	370	371
B-0315			61	384	385
B-0316			75	368	369
B-0317			62	366	367
B-0318			52	388	389
B-0319			53	424	425
B-0320			50	424	425
B-0321			54	442	443

Example#	R <sup>2</sup>	R <sup>J</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0322			64	474	475
B-0323			58	474	475
B-0324			60	422	423
B-0325			64	422	423
B-0326			58	422	423
B-0327			63	378	379
B-0328			68	389	390
B-0329			63	362	363
B-0330			48	376	377
B-0331			66	424	425

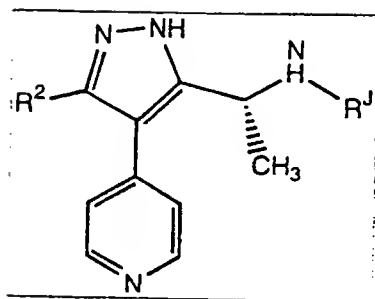
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0332			61	442	443
B-0333			60	458	459
B-0334			55	502	503
B-0335			60	454	455
B-0336			100	500	501
B-0337			65	458	-
B-0338			69	502	503
B-0339			69	454	-
B-0340			77	492	493
B-0341			64	458	459

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0342			41	438	-
B-0343			63	430	431
B-0344			96	464	465
B-0345			62	507	508
B-0346			56	497	498
B-0347			61	341	342
B-0348			3	367	-
B-0349			57	403	404
B-0350			57	481	482
B-0351			31	355	356

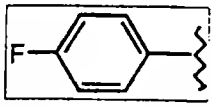
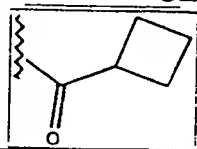
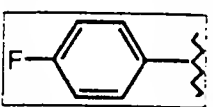
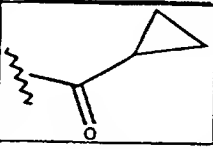
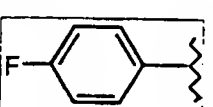
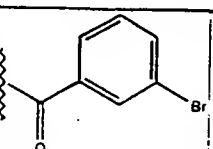
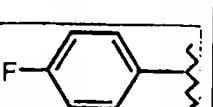
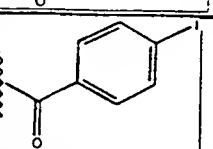
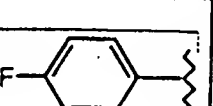
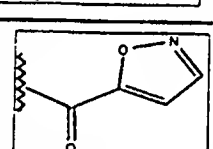
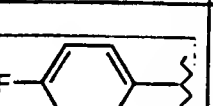
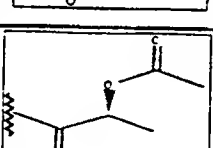
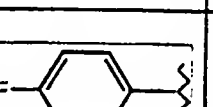
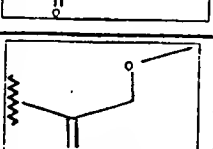
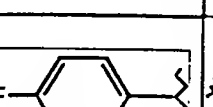
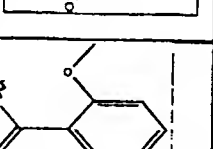
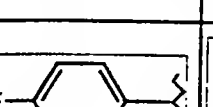
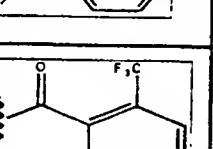

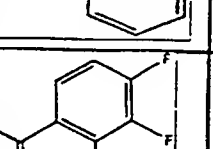
623

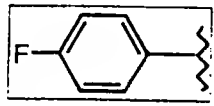
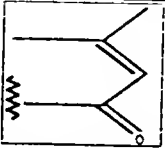
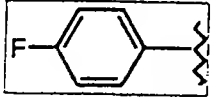
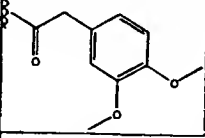
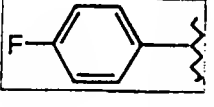
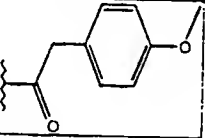
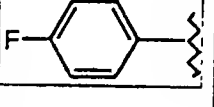
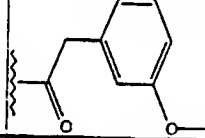
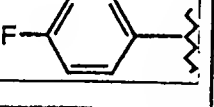
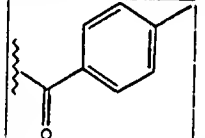
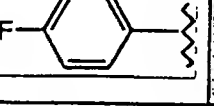
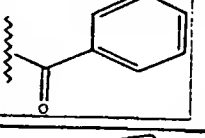
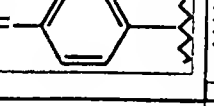
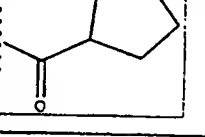
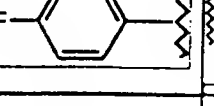
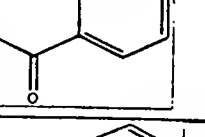
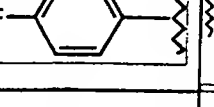
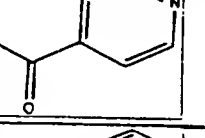
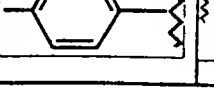
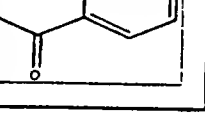
Example#	R <sup>2</sup>	R <sup>J</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0352			51	397	398

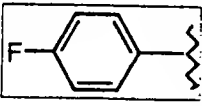
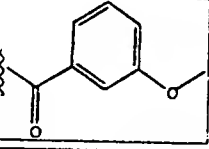
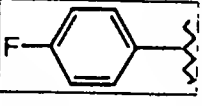
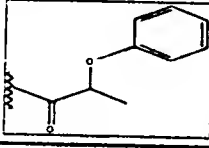
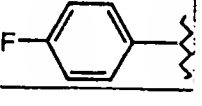
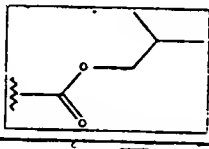
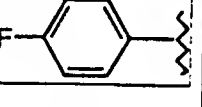
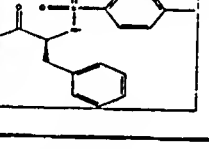
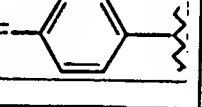
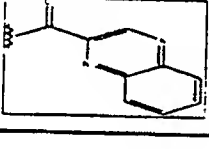
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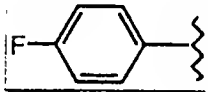
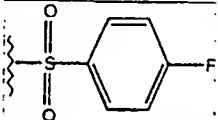
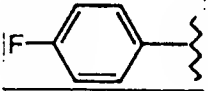
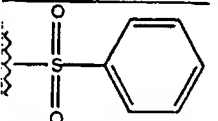
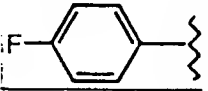
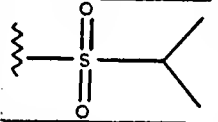
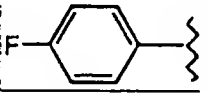
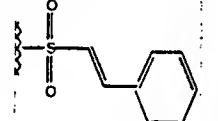
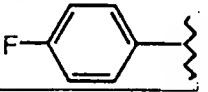
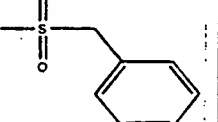
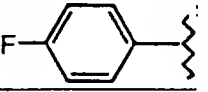
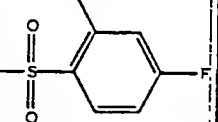
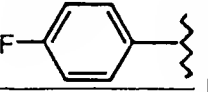
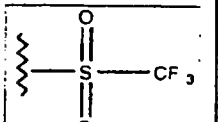


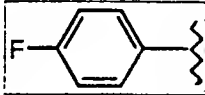
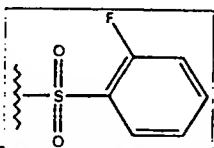
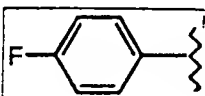
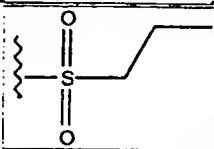
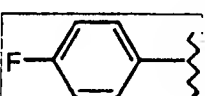
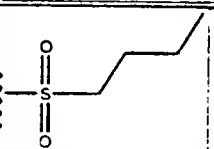
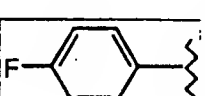
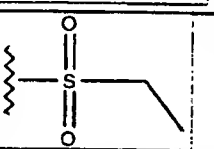
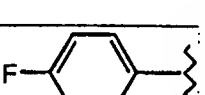
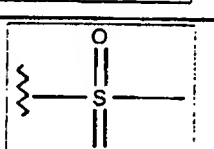
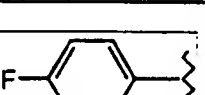
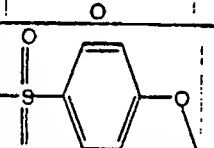
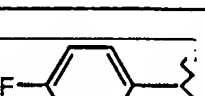
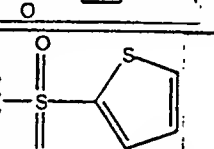

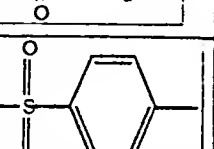

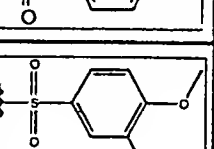

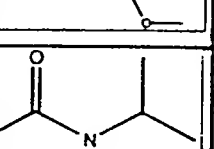
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0353			71	382	383
B-0354			35	512	513
B-0355			37	352	353
B-0356			57	404	405
B-0357			88	366	367
B-0358			88	410	411
B-0359			100	324	325

Example#	R <sup>2</sup>	R <sup>3</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0360			56	364	365
B-0361			70	350	351
B-0362			100	464	465
B-0363			73	512	513
B-0364			88	377	378
B-0365			70	396	397
B-0366			100	354	355
B-0367			71	416	417
B-0368			86	454	455
B-0369			40	440	441

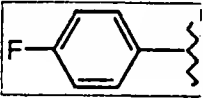
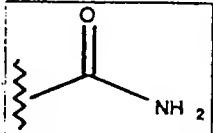
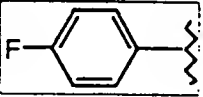
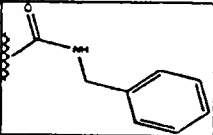
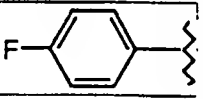
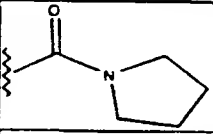
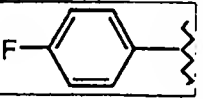
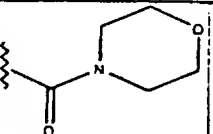
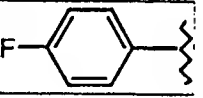
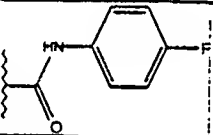
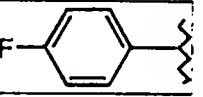
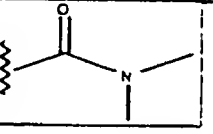
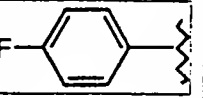
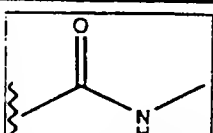
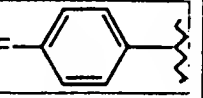

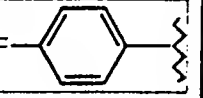
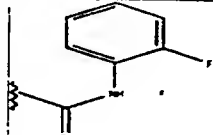
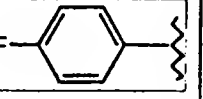
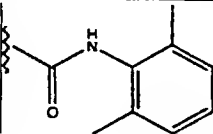
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0370			94	364	365
B-0371			88	460	461
B-0372			69	430	431
B-0373			100	430	431
B-0374			75	400	401
B-0375			74	386	387
B-0376			53	378	379
B-0377			71	387	388
B-0378			69	387	388
B-0379			66	387	388

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0380			85	416	417
B-0381			93	430	431
B-0382			84	382	383
B-0383			74	583	584
B-0384			63	438	439

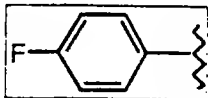
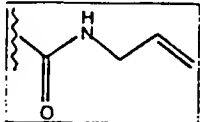
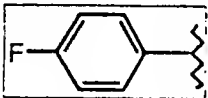
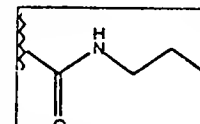
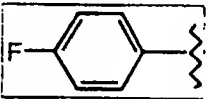
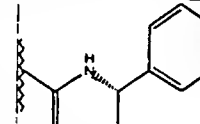
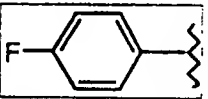
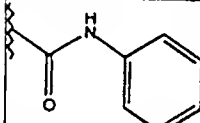
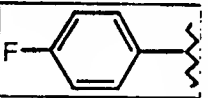
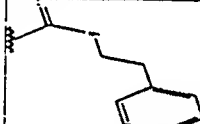
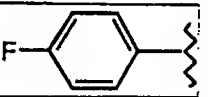
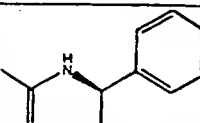
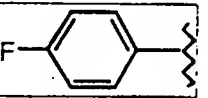
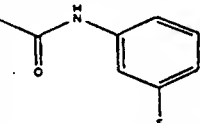
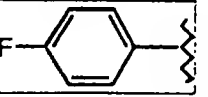
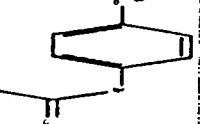
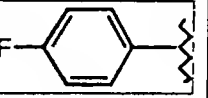
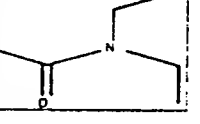
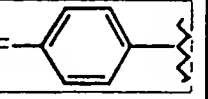
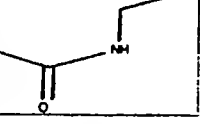
Example#	R <sup>2</sup>	R <sup>J</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0385			83	440	441
B-0386			99	422	423
B-0387			47	388	389
B-0388			100	448	449
B-0389			71	436	437
B-0390			100	458	459
B-0391			45	414	415

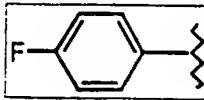
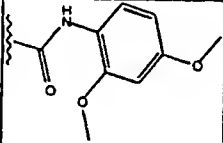
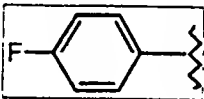
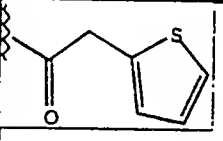
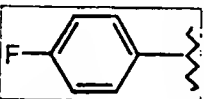
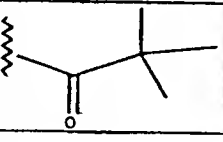
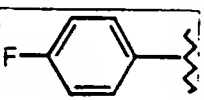
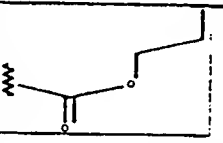
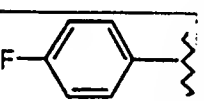
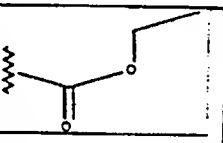
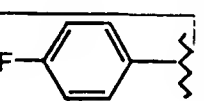
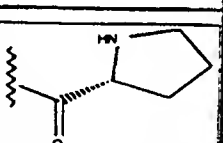
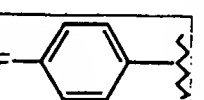
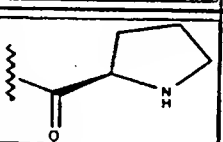
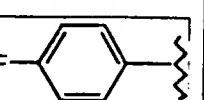
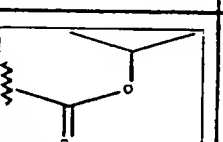
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0392			100	440	441
B-0393			75	388	389
B-0394			92	402	403
B-0395			87	374	375
B-0396			86	360	361
B-0397			81	452	453
B-0398			88	428	429
B-0399			99	436	437
B-0400			82	482	483
B-0401			94	367	368

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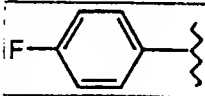
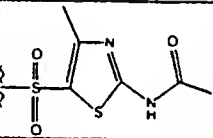
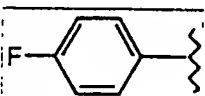
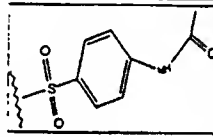
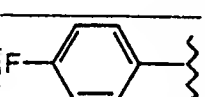
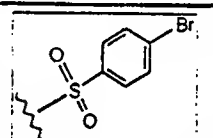
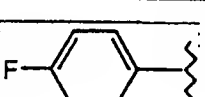
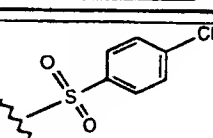
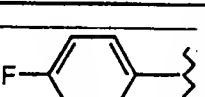
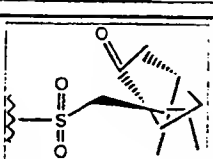
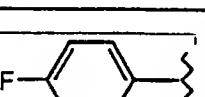
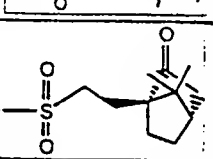
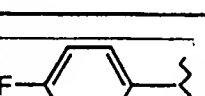
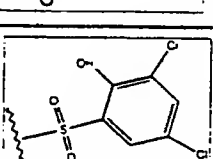
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0402			73	325	326
B-0403			91	415	416
B-0404			41	379	380
B-0405			88	395	396
B-0406			100	419	420
B-0407			52	353	354
B-0408			83	339	340
B-0409			74	415	416
B-0410			100	419	420
B-0411			94	429	430

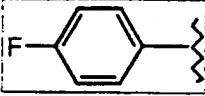
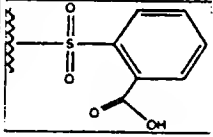
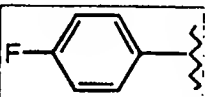
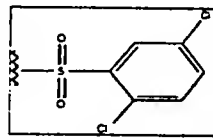
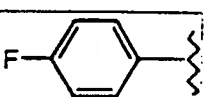
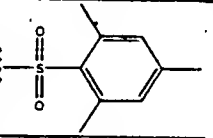
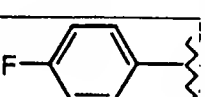
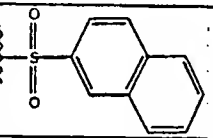
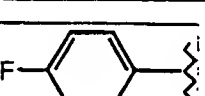
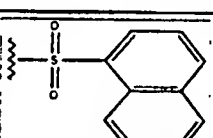

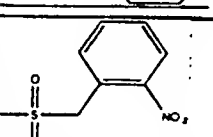
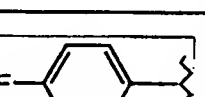
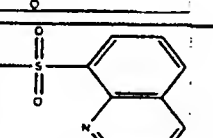
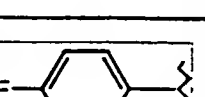
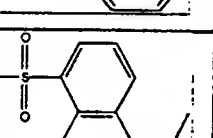

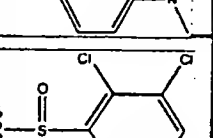

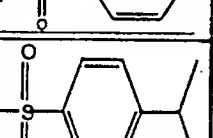
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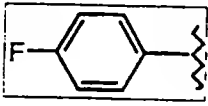
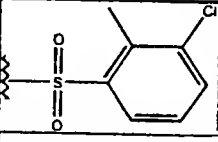
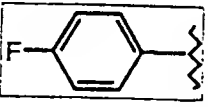
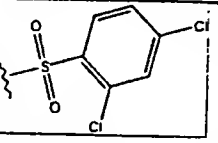
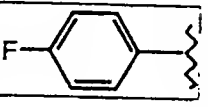
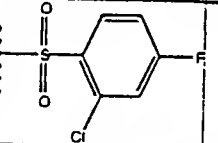
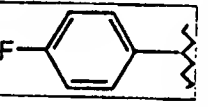
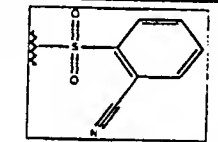
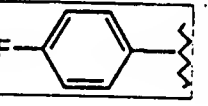
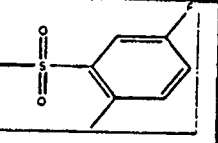
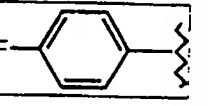
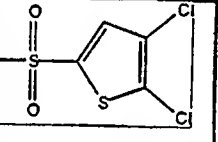
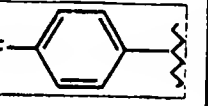
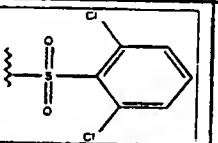
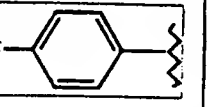
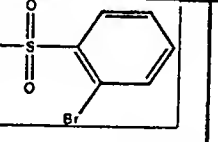
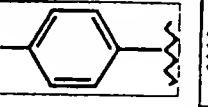
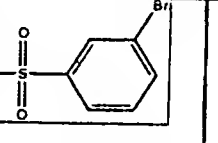
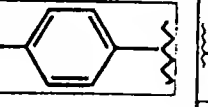
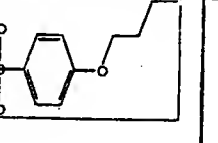
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0412			91	365	366
B-0413			79	367	368
B-0414			85	429	430
B-0415			82	401	402
B-0416			93	429	430
B-0417			97	429	430
B-0418			100	419	420
B-0419			100	431	432
B-0420			36	381	382
B-0421			96	353	354

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0422			100	461	462
B-0423			100	406	407
B-0424			76	366	367
B-0425			21	368	369
B-0426			100	354	355
B-0427			100	379	380
B-0428			100	379	380
B-0429			86	368	369

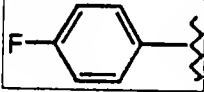
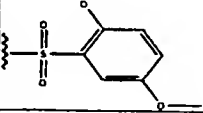
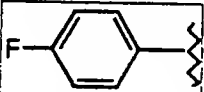
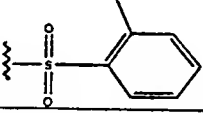
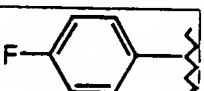
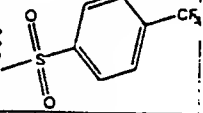
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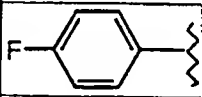
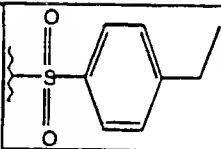
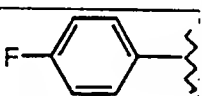
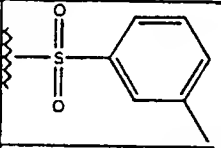
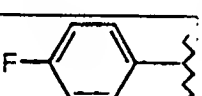
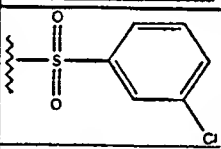
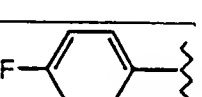
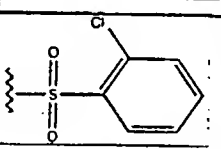
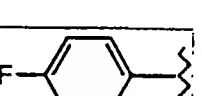
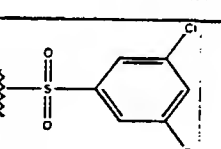
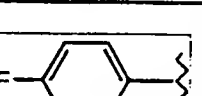
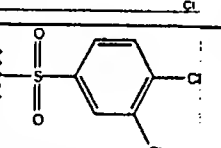
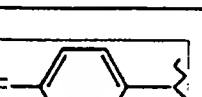
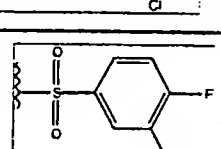
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0430			51	500	501
B-0431			76	479	480
B-0432			90	500	501
B-0433			96	456	457
B-0434			75	496	497
B-0435			52	496	497
B-0436			73	506	

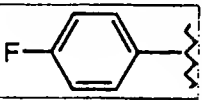
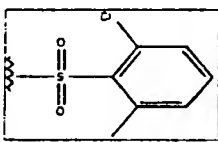
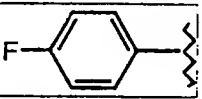
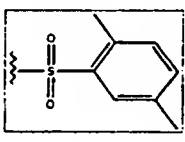
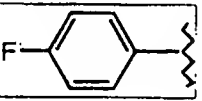
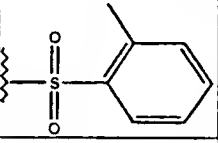
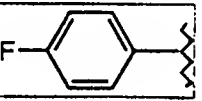
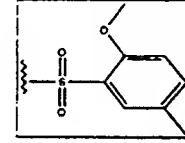
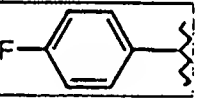
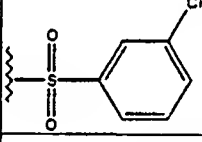
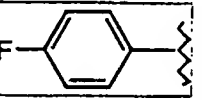
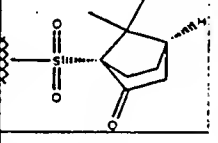
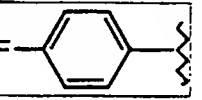
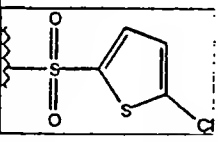
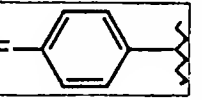
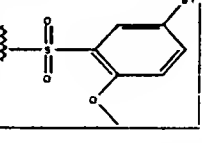
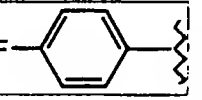
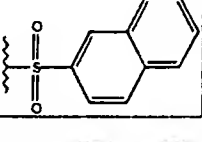
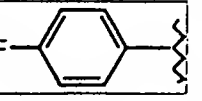
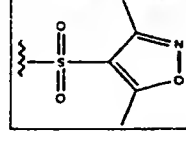
Example#	R <sup>2</sup>	R <sup>J</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0437			19	466	
B-0438			100	490	491
B-0439			67	464	465
B-0440			96	472	473
B-0441			87	472	473
B-0442			72	481	482
B-0443			66	473	474
B-0444			80	515	516
B-0445			94	490	491
B-0446			84	464	465

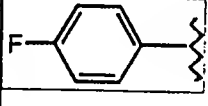
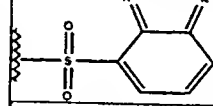
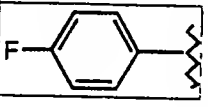
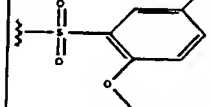
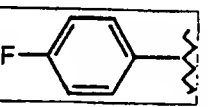
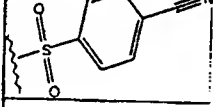
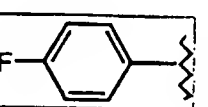
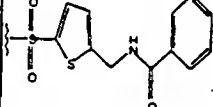
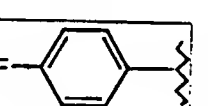
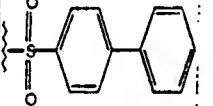
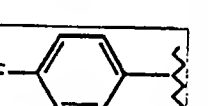
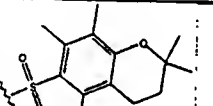
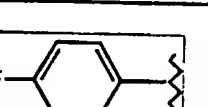
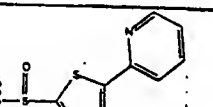
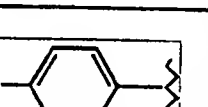
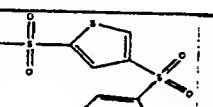
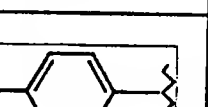
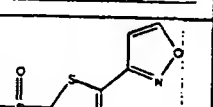
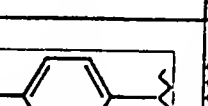
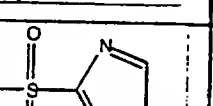
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0447			89	470	471
B-0448			100	490	491
B-0449			100	474	475
B-0450			100	447	448
B-0451			100	454	455
B-0452			95	496	497
B-0453			100	490	491
B-0454			100	500	501
B-0455			96	500	501
B-0456			89	494	495

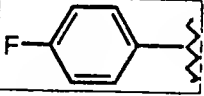
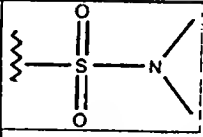
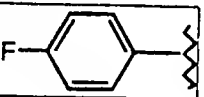
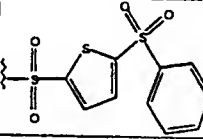
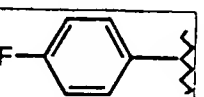
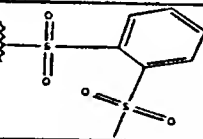
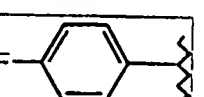
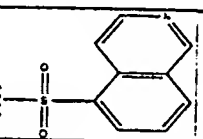
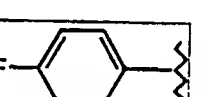
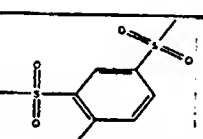
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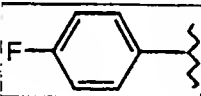
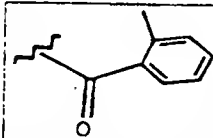
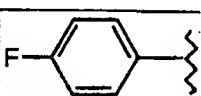
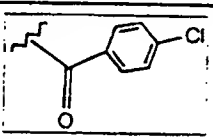
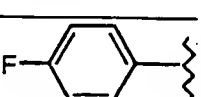
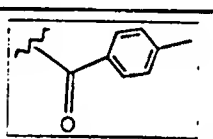
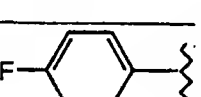
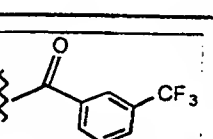
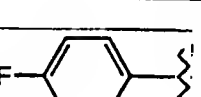
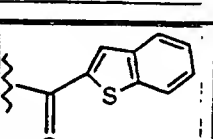
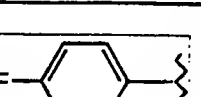
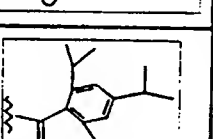
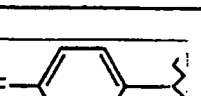
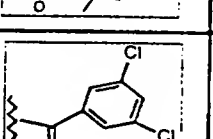
Example#	R <sup>2</sup>	R <sup>J</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0457			93	482	483
B-0458			100	490	491
B-0459			100	490	491

Example#	R <sup>2</sup>	R <sup>J</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0460			93	450	451
B-0461			84	452	453
B-0462			96	456	457
B-0463			66	456	457
B-0464			69	490	491
B-0465			86	490	491
B-0466			78	474	475

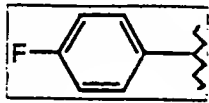
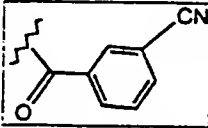
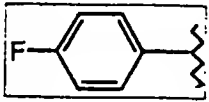
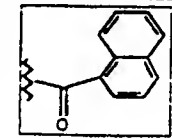
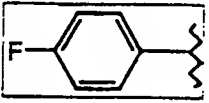
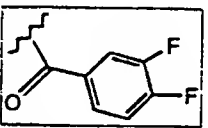
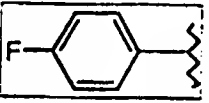
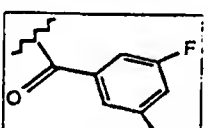
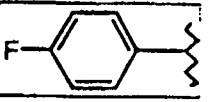
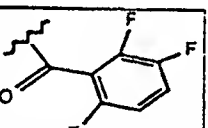
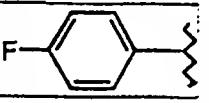
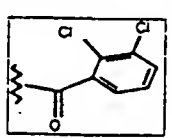
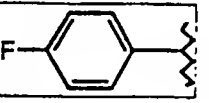
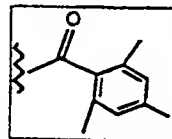
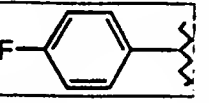
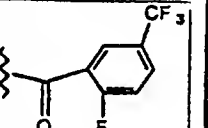
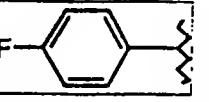
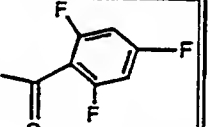
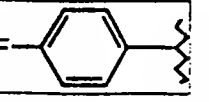
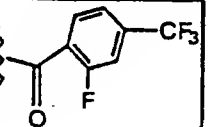
Example#	R <sup>2</sup>	R <sup>J</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0467			78	470	471
B-0468			91	450	451
B-0469			85	436	437
B-0470			99	466	467
B-0471			100	490	491
B-0472			37	482	483
B-0473			92	462	463
B-0474			99	530	532
B-0475			55	472	473
B-0476			89	441	442

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0477			79	464	465
B-0478			92	486	487
B-0479			97	447	448
B-0480			75	561	562
B-0481			74	498	499
B-0482			57	548	549
B-0483			83	505	506
B-0484			100	568	569
B-0485			100	495	496
B-0486			100	426	427

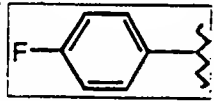
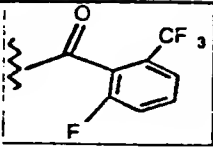
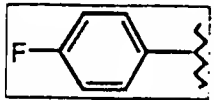
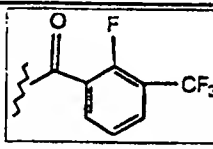
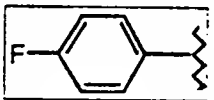
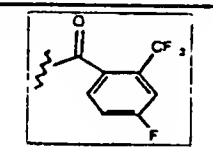
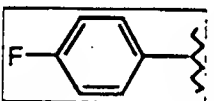
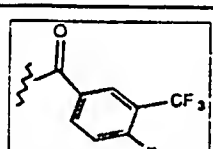
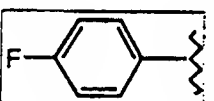
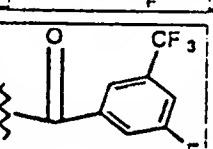
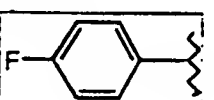
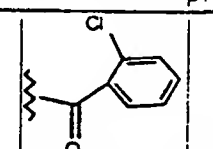
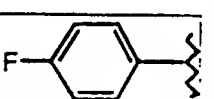
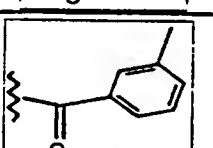
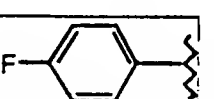
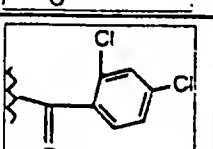
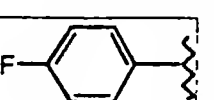
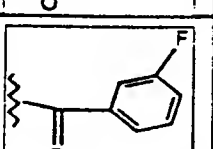
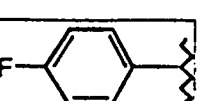
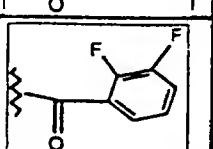
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0487			32	389	390
B-0488			100	568	569
B-0489			91	500	501
B-0490			40	473	474
B-0491			73	514	515

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0492			89	400	401
B-0493			100	420	421
B-0494			100	400	401
B-0495			100	454	455
B-0496			100	442	443
B-0497			50	512	513
B-0498			100	454	455

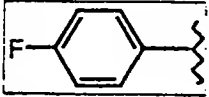
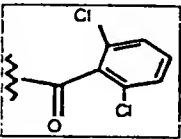
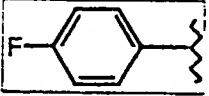
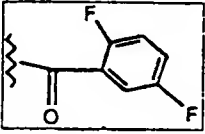
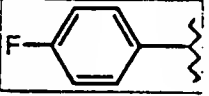
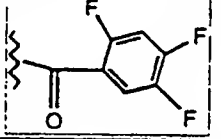
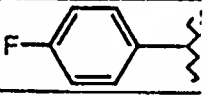
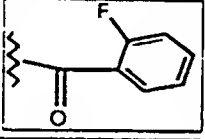
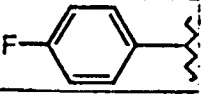
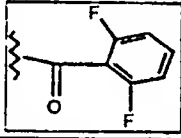
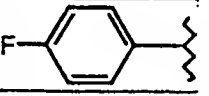
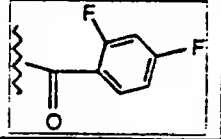
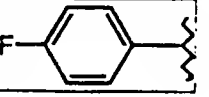
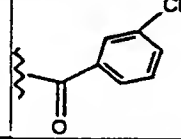
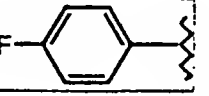
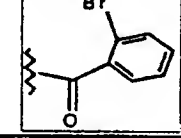
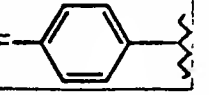
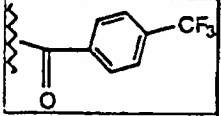
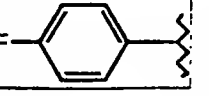
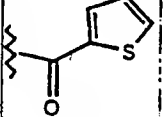
642

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0499			98	411	412
B-0500			100	436	437
B-0501			100	422	423
B-0502			100	422	423
B-0503			92	440	441
B-0504			67	454	455
B-0505			68	428	429
B-0506			98	472	473
B-0507			82	440	441
B-0508			99	472	473

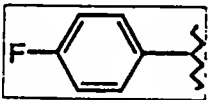
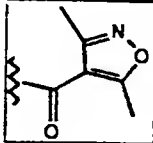
643

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0509			100	472	473
B-0510			96	472	473
B-0511			100	472	473
B-0512			100	472	473
B-0513			100	472	473
B-0514			100	420	421
B-0515			100	400	401
B-0516			100	454	455
B-0517			100	404	405
B-0518			99	422	423

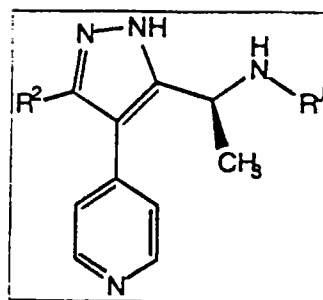
644

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0519			100	454	455
B-0520			98	422	423
B-0521			99	440	441
B-0522			88	404	405
B-0523			100	422	423
B-0524			100	422	423
B-0525			100	420	421
B-0526			100	464	465
B-0527			100	454	455
B-0528			100	392	393

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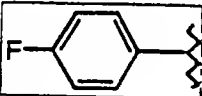
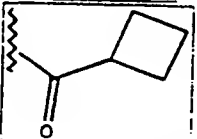
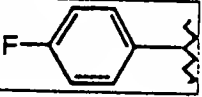
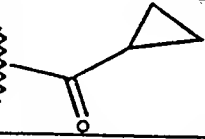
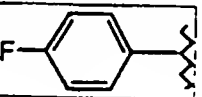
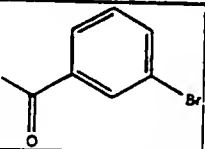
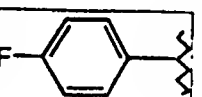
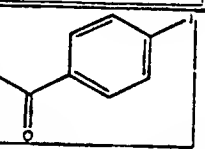
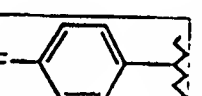
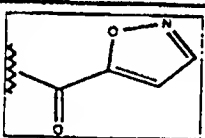
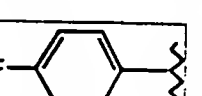
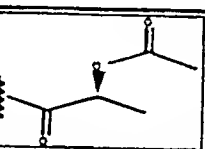
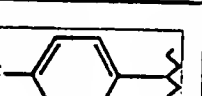
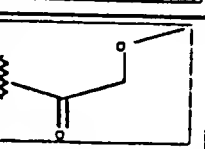
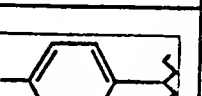
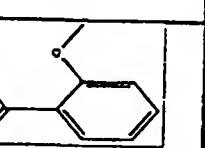
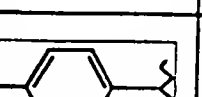
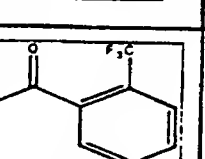
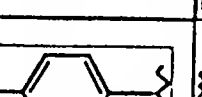
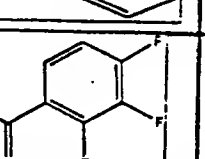
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0529			94	405	406

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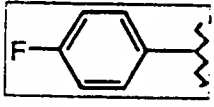
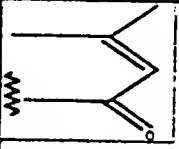
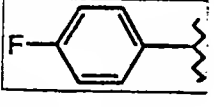
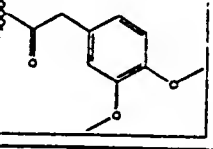
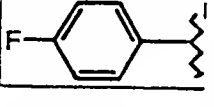
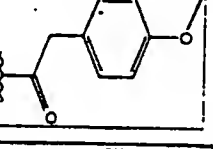
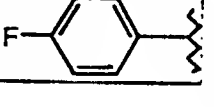
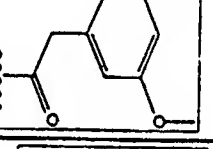
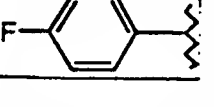
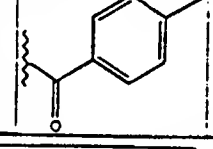
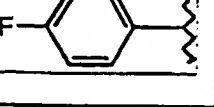
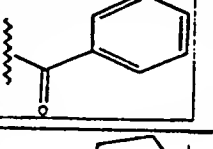
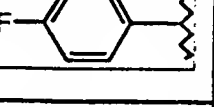
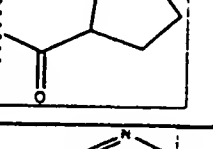
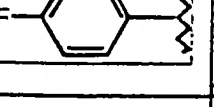
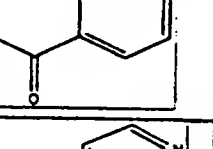
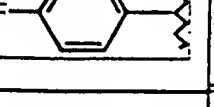
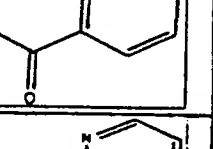
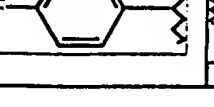
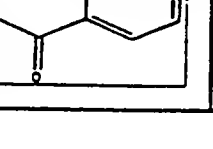


Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0530			67	382	383
B-0531			66	512	513
B-0532			37	352	353
B-0533			56	404	405
B-0534			100	366	367
B-0535			100	410	411
B-0536			41	324	325

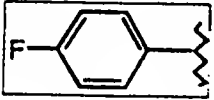
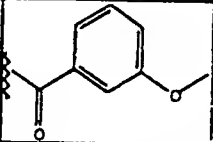
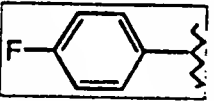
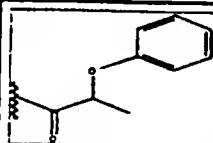
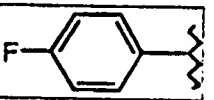
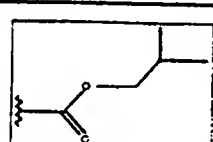
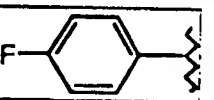
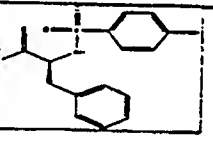
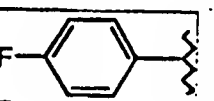
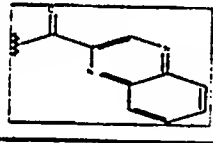
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Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0537			100	364	365
B-0538			29	350	351
B-0539			70	464	465
B-0540			50	512	513
B-0541			61	377	378
B-0542			61	396	397
B-0543			59	354	355
B-0544			45	416	417
B-0545			100	454	455
B-0546			44	440	441

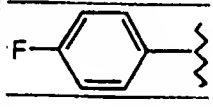
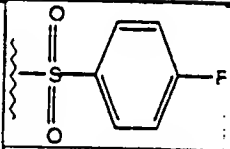
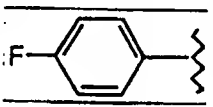
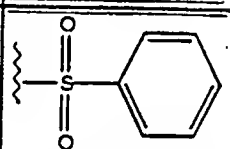
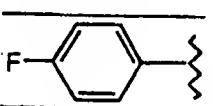
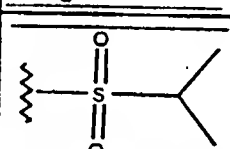
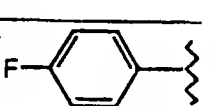
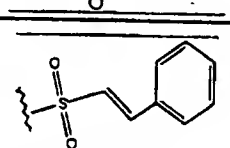
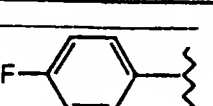
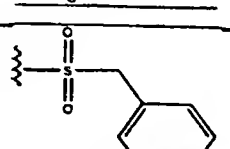
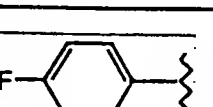
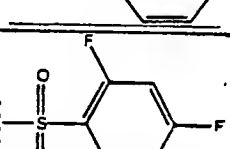
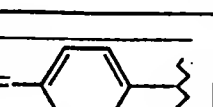
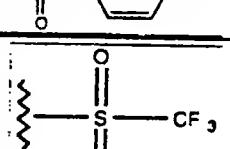
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Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0547			64	364	365
B-0548			89	460	461
B-0549			100	430	431
B-0550			100	430	431
B-0551			81	400	401
B-0552			38	386	387
B-0553			31	378	379
B-0554			100	387	388
B-0555			66	387	388
B-0556			32	387	388

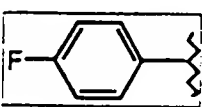
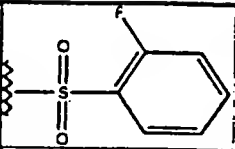
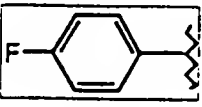
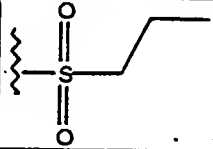
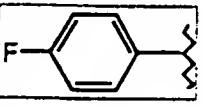
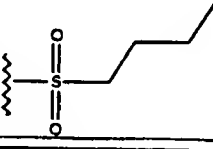
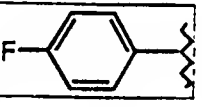
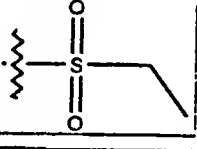
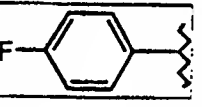
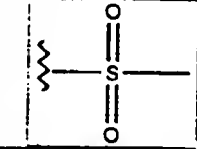
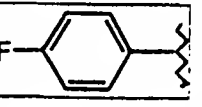
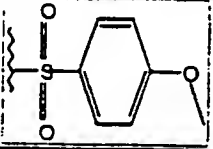
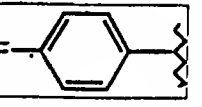
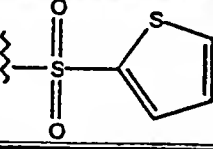
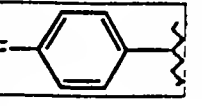
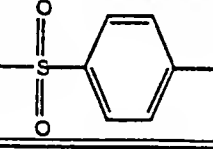
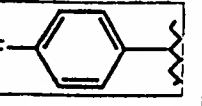
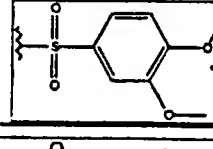
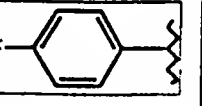
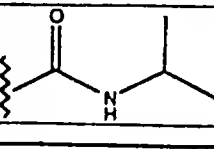
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Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0557			70	416	417
B-0558			57	430	431
B-0559			74	382	383
B-0560			36	583	584
B-0561			51	438	439

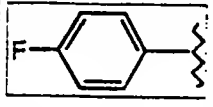
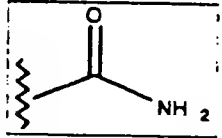
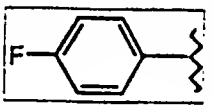
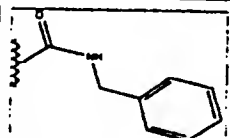
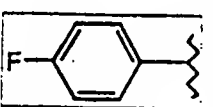
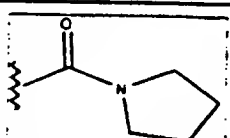
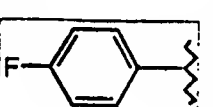
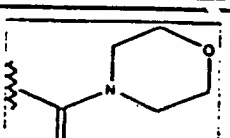
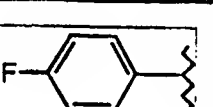
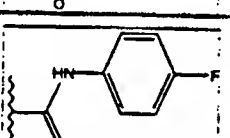
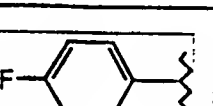
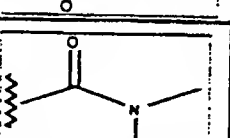
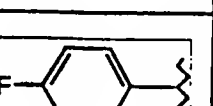
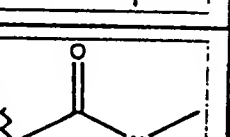
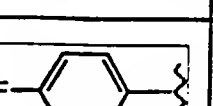
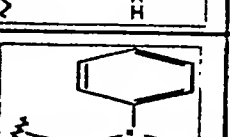
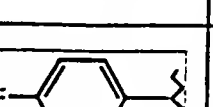
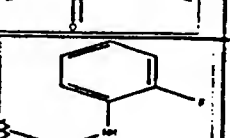
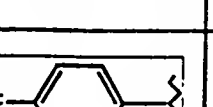
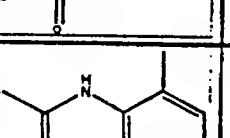
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Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0562			88	440	441
B-0563			68	422	423
B-0564			47	388	389
B-0565			100	448	449
B-0566			76	436	437
B-0567			99	458	459
B-0568			45	414	415

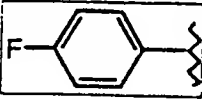
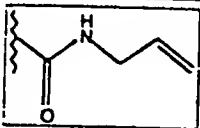
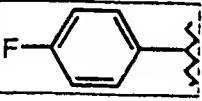
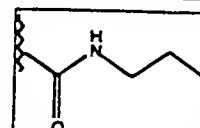
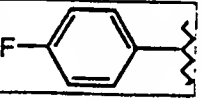
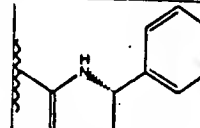
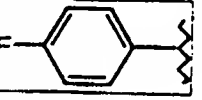
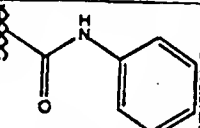
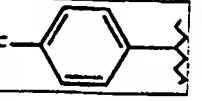

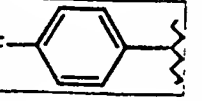
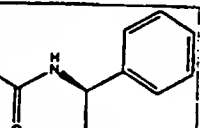
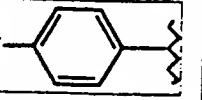
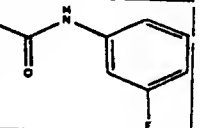
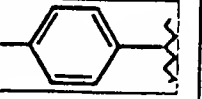

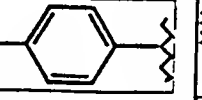
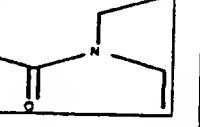
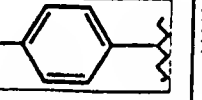

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Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0569			88	440	441
B-0570			61	388	389
B-0571			58	402	403
B-0572			75	374	375
B-0573			72	360	361
B-0574			97	452	453
B-0575			71	428	429
B-0576			88	436	437
B-0577			72	482	483
B-0578			89	367	368

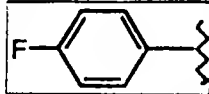
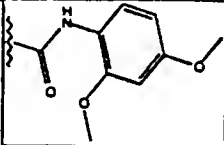
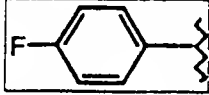
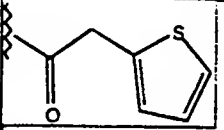
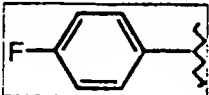
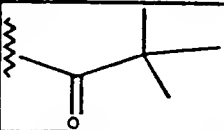
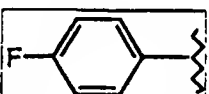
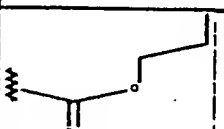
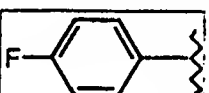
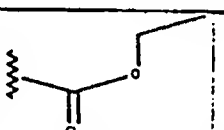
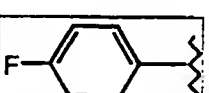
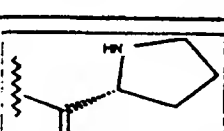
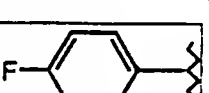
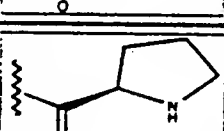
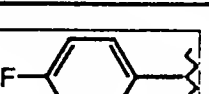
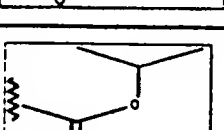
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Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0579			100	325	326
B-0580			75	415	416
B-0581			44	379	380
B-0582			75	395	396
B-0583			80	419	420
B-0584			57	353	354
B-0585			83	339	340
B-0586			71	415	416
B-0587			100	419	420
B-0588			94	429	430

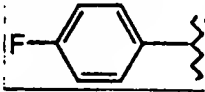
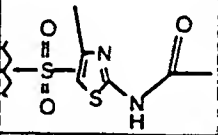
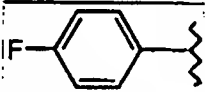
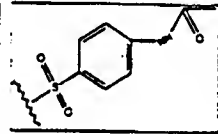
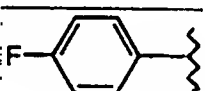
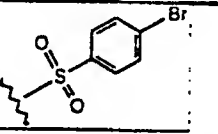
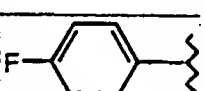
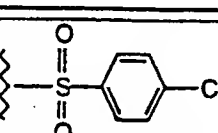
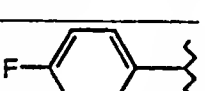
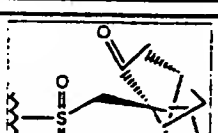
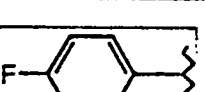
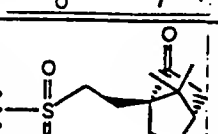
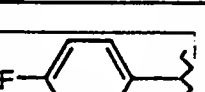
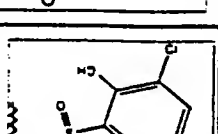
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Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0589			78	365	366
B-0590			82	367	368
B-0591			72	429	430
B-0592			82	401	402
B-0593			88	429	430
B-0594			100	429	430
B-0595			99	419	420
B-0596			93	431	432
B-0597			40	381	382
B-0598			93	353	354

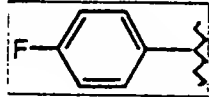
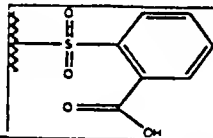
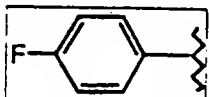
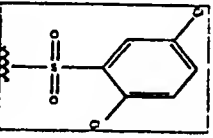
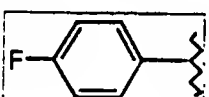
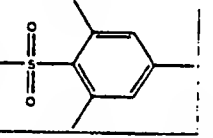
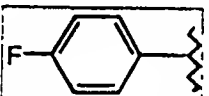
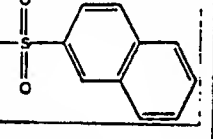
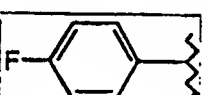
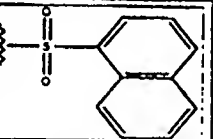
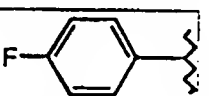
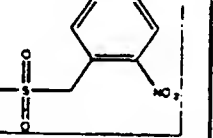
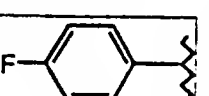
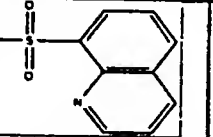
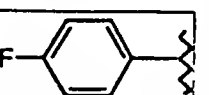
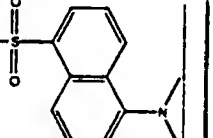
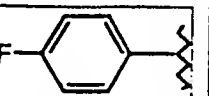
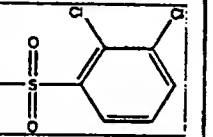
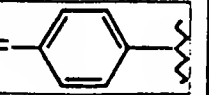
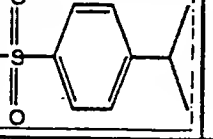
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Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0599			100	461	462
B-0600			98	406	407
B-0601			66	366	367
B-0602			25	368	369
B-0603			90	354	355
B-0604			86	379	380
B-0605			87	379	380
B-0606			72	368	369

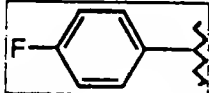
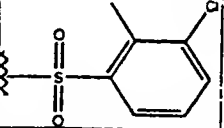
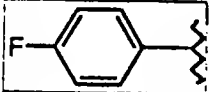
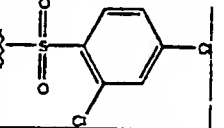
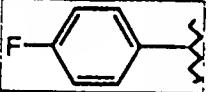
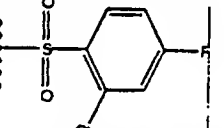
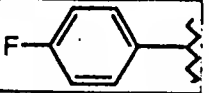

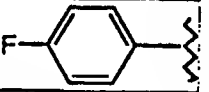
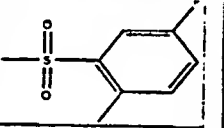
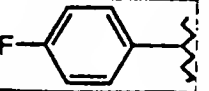
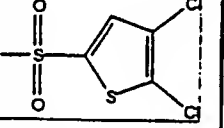
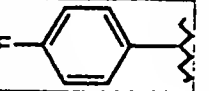
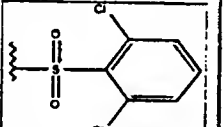
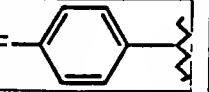
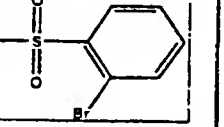
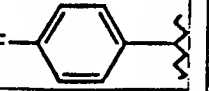
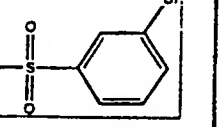
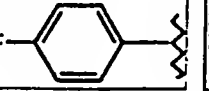
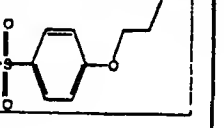
655

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0607			34	500	501
B-0608			100	479	480
B-0609			82	500	501
B-0610			100	456	457
B-0611			76	496	497
B-0612			69	496	497
B-0613			61	506	

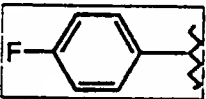
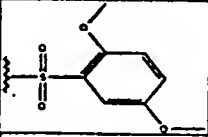
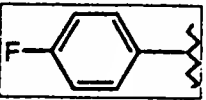
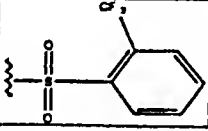
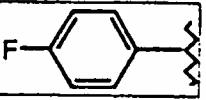
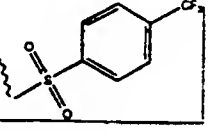
656

Example#	R <sup>2</sup>	R <sup>J</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0614			18	466	
B-0615			100	490	491
B-0616			77	464	465
B-0617			93	472	473
B-0618			84	472	473
B-0619			71	481	482
B-0620			89	473	474
B-0621			68	515	516
B-0622			70	490	491
B-0623			92	464	465

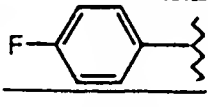
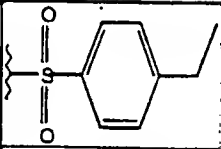
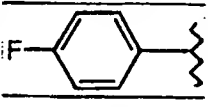
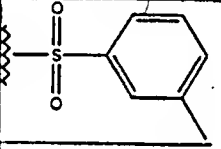
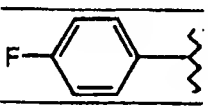
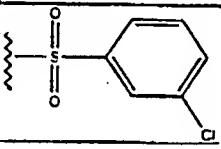
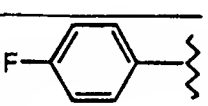
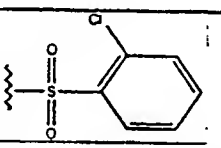
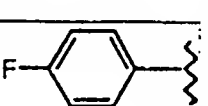
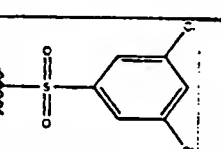
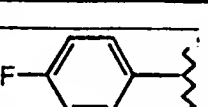
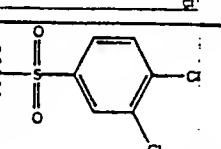
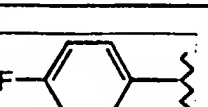
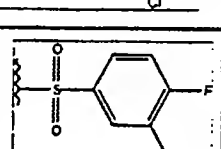
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Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0624			98	470	471
B-0625			96	490	491
B-0626			100	474	475
B-0627			100	447	448
B-0628			64	454	455
B-0629			100	496	497
B-0630			85	490	491
B-0631			75	500	501
B-0632			83	500	501
B-0633			58	494	495

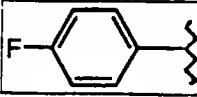
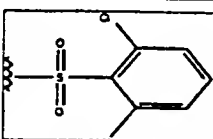
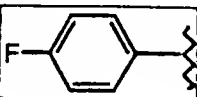
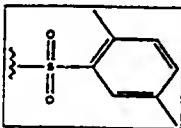
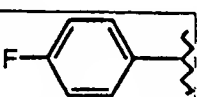
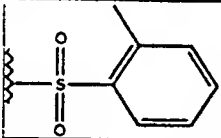
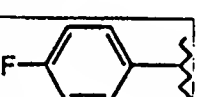
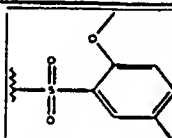
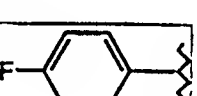
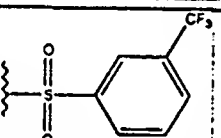
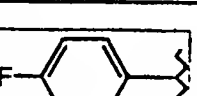
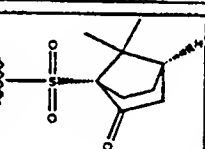
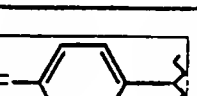
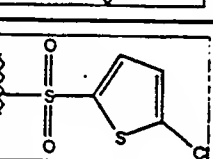
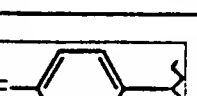
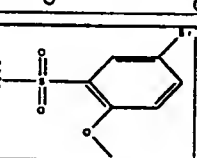

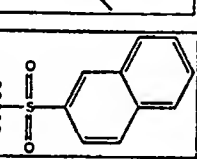

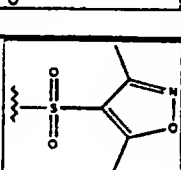
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Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0634			63	482	483
B-0635			95	490	491
B-0636			100	490	491

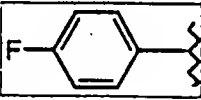
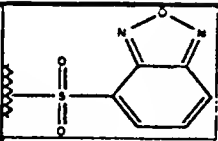
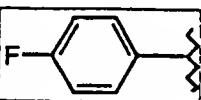
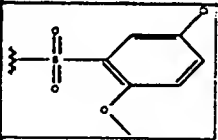
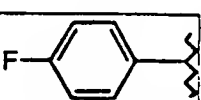
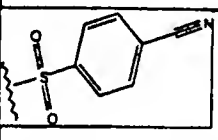
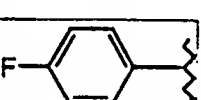
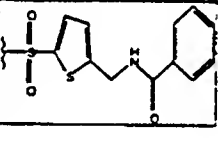
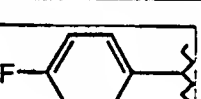
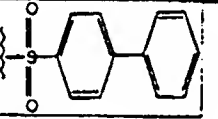
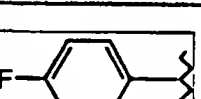
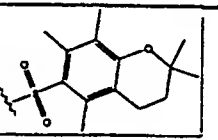
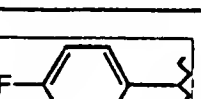
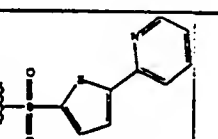
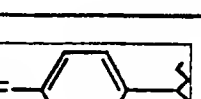
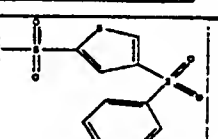

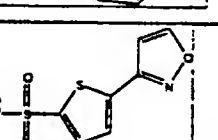

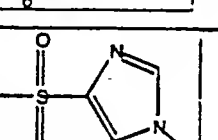
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Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0637			91	450	451
B-0638			96	436	437
B-0639			100	456	457
B-0640			100	456	457
B-0641			88	490	491
B-0642			99	490	491
B-0643			92	474	475

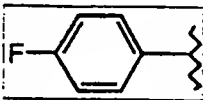
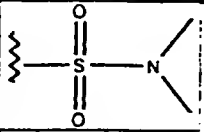
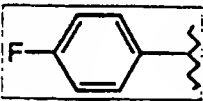
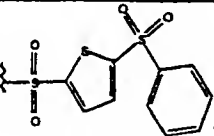
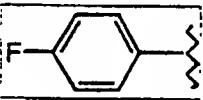
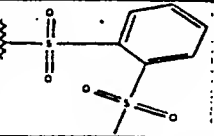
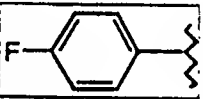
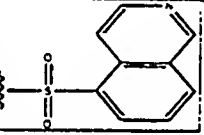
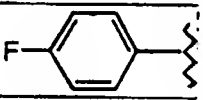
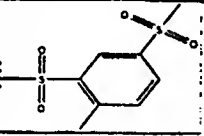
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Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0644			100	470	471
B-0645			92	450	451
B-0646			100	436	437
B-0647			90	466	467
B-0648			94	490	491
B-0649			57	482	
B-0650			82	462	463
B-0651			100	530	531
B-0652			53	472	
B-0653			84	441	442

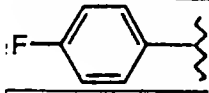
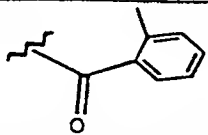
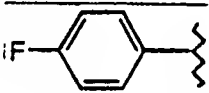
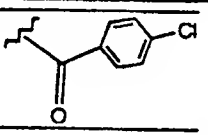
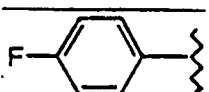
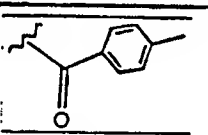
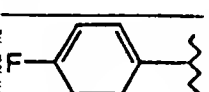
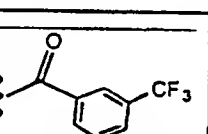
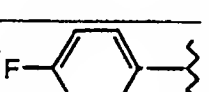
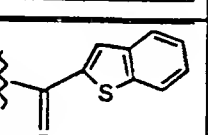
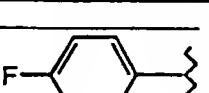
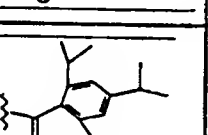
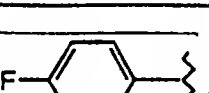
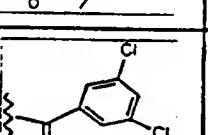
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Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0654			92	464	465
B-0655			100	486	487
B-0656			98	447	448
B-0657			85	561	562
B-0658			92	498	499
B-0659			46	548	549
B-0660			80	505	506
B-0661			100	568	569
B-0662			98	495	496
B-0663			74	426	427

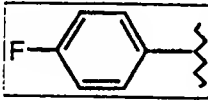
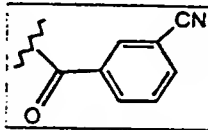
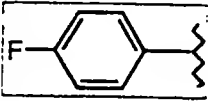
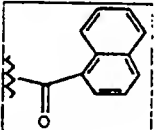
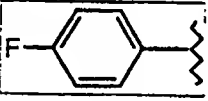
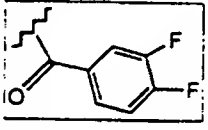
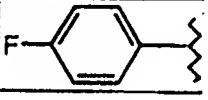
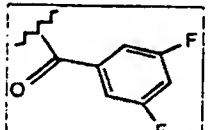
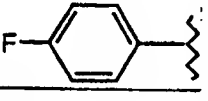
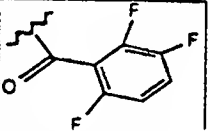
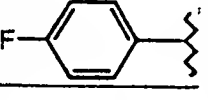
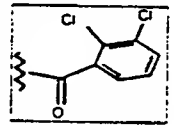
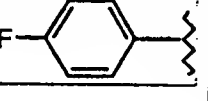
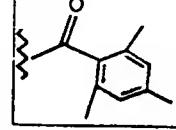
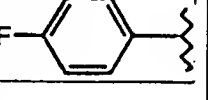
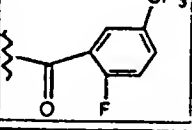
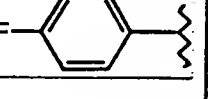
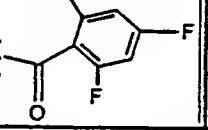
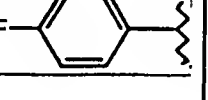
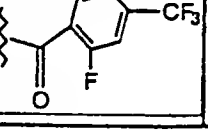
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Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0664			30	389	390
B-0665			100	568	569
B-0666			93	500	501
B-0667			54	473	474
B-0668			66	514	515

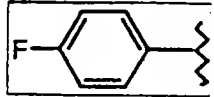
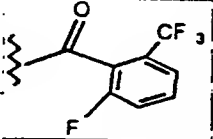
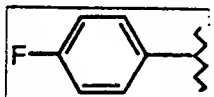
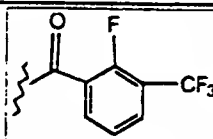
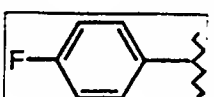
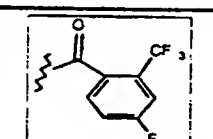
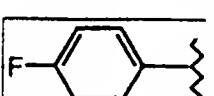
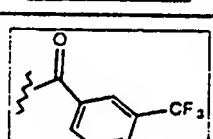
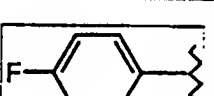
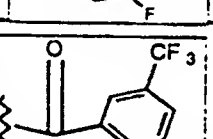
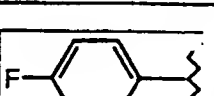
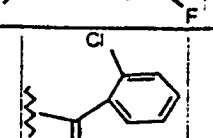
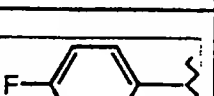
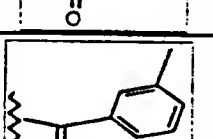

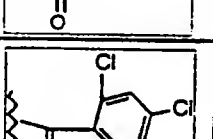



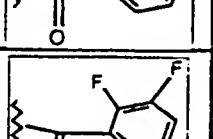
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Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0669			65	400	401
B-0670			45	420	421
B-0671			43	400	401
B-0672			45	454	455
B-0673			41	442	443
B-0674			16	512	513
B-0675			39	454	455

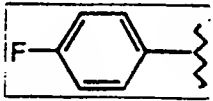
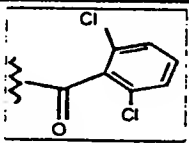
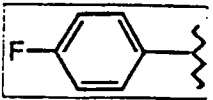
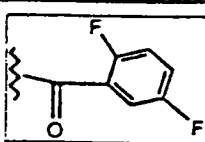
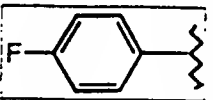
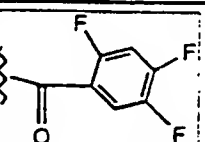
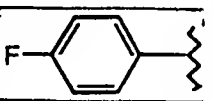
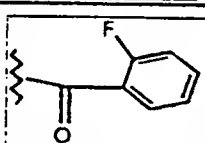
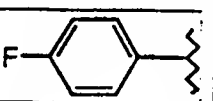
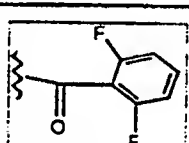
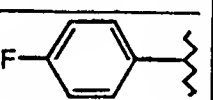
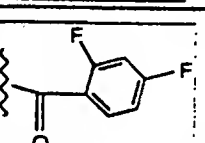
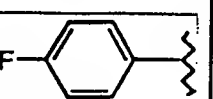
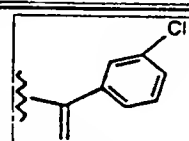
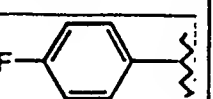
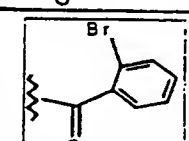
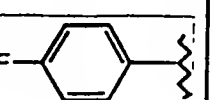
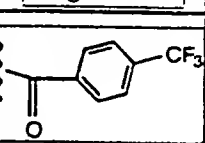
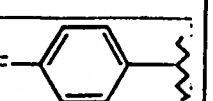
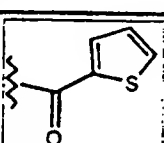
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Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0676			34	411	412
B-0677			46	436	437
B-0678			37	422	423
B-0679			34	422	423
B-0680			60	440	441
B-0681			31	454	455
B-0682			37	428	429
B-0683			46	472	473
B-0684			50	440	441
B-0685			44	472	473

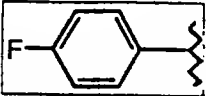
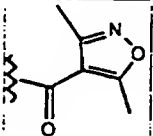
665

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0686			66	472	473
B-0687			57	472	473
B-0688			52	472	473
B-0689			42	472	473
B-0690			34	472	473
B-0691			52	420	421
B-0692			41	400	401
B-0693			56	454	455
B-0694			38	404	405
B-0695			43	422	423

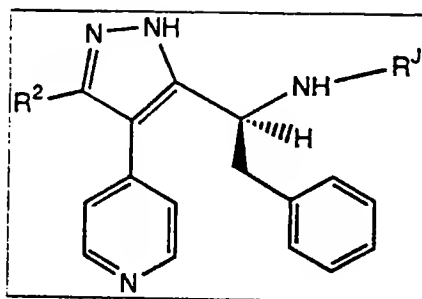
666

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0696			57	454	455
B-0697			51	422	423
B-0698			59	440	441
B-0699			46	404	405
B-0700			47	422	423
B-0701			46	422	423
B-0702			43	420	421
B-0703			57	464	465
B-0704			44	454	455
B-0705			33	392	393

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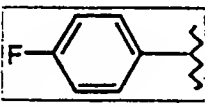
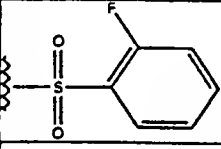
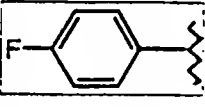
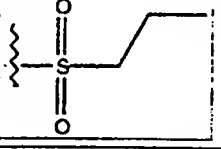
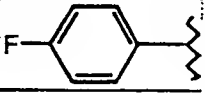
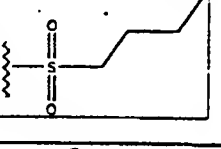
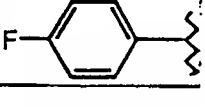
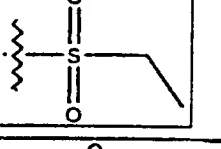
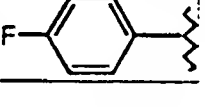
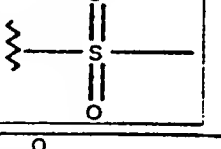
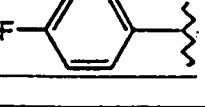
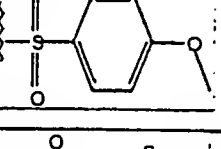
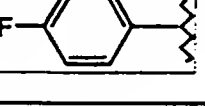
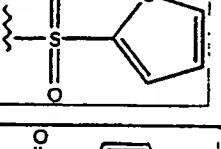
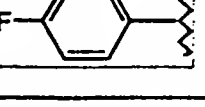
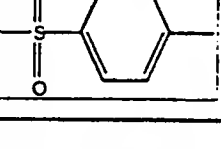
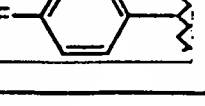
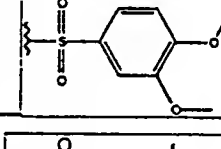
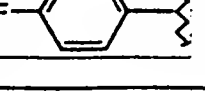
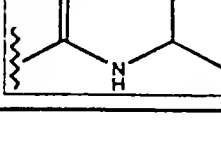
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0706			35	405	406

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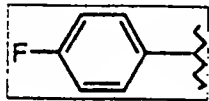
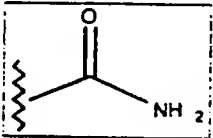
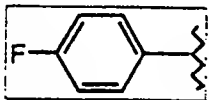
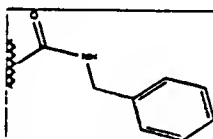
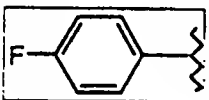
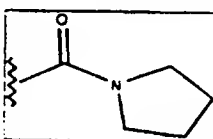
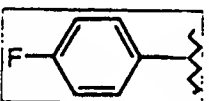
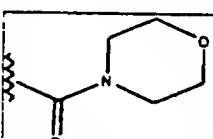
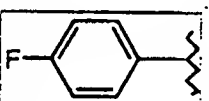
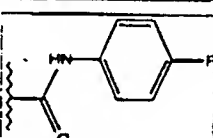
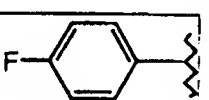
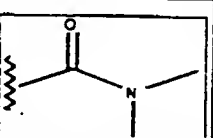
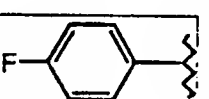
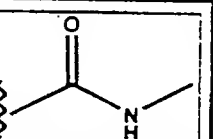
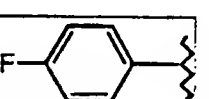

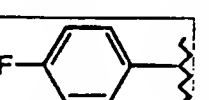
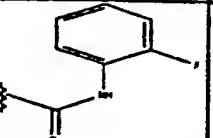
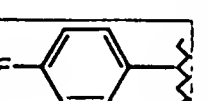
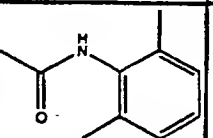


Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0707			76	516	517
B-0708			61	498	499
B-0709			37	464	465
B-0710			76	524	525
B-0711			75	512	513
B-0712			91	534	535
B-0713			42	490	491

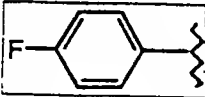
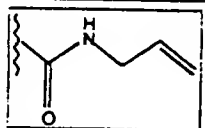
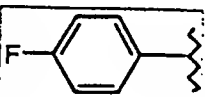
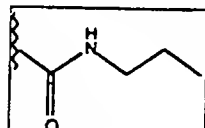
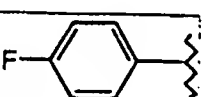
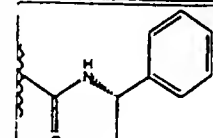
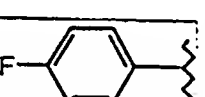
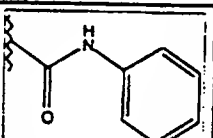
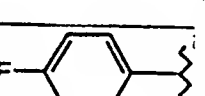
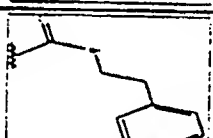
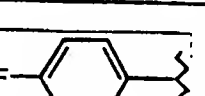
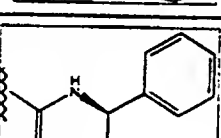
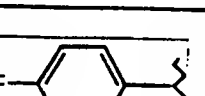
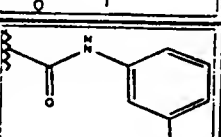
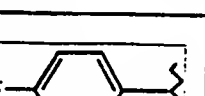
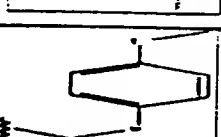

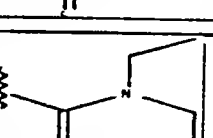

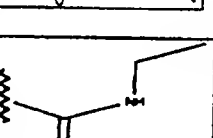
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Example#	R <sup>2</sup>	R <sup>J</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0714			87	516	517
B-0715			60	464	465
B-0716			59	478	479
B-0717			61	450	451
B-0718			65	436	437
B-0719			84	528	529
B-0720			69	504	505
B-0721			63	512	513
B-0722			88	558	559
B-0723			68	443	444

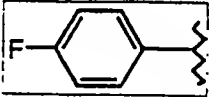
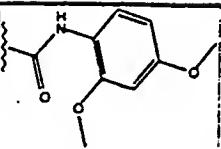
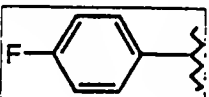
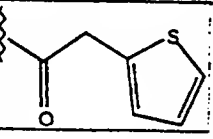
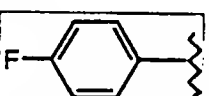
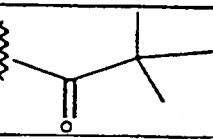
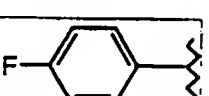
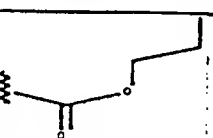
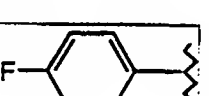
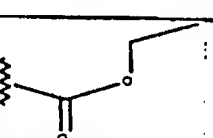
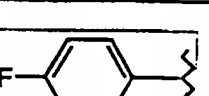
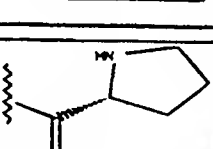
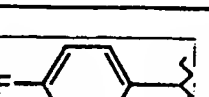
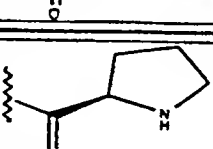
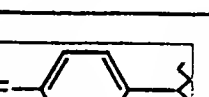
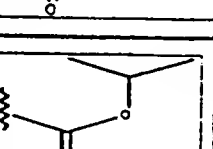
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Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0724			75	401	402
B-0725			83	491	492
B-0726			24	455	456
B-0727			67	471	472
B-0728			89	495	496
B-0729			38	429	430
B-0730			76	415	416
B-0731			60	491	492
B-0732			86	495	496
B-0733			81	505	506

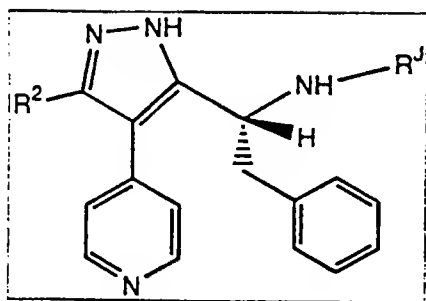
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Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0734			87	441	442
B-0735			83	443	444
B-0736			91	505	506
B-0737			9	477	-
B-0738			87	505	506
B-0739			82	505	506
B-0740			85	495	496
B-0741			68	507	508
B-0742			14	457	-
B-0743			77	429	430

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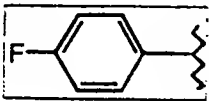
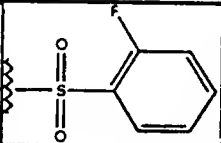
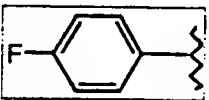
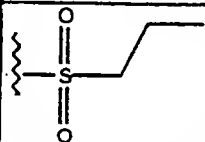
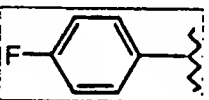
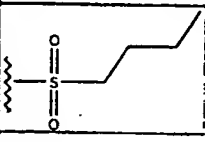
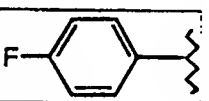
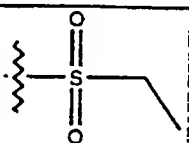
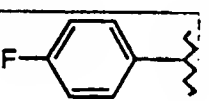
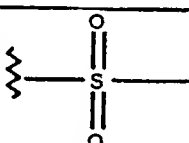
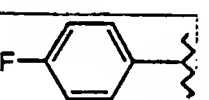
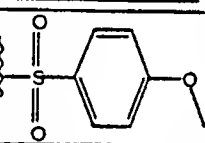
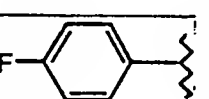
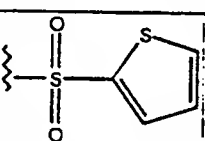
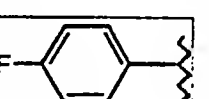
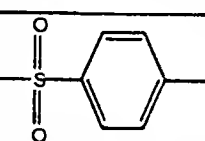
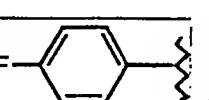
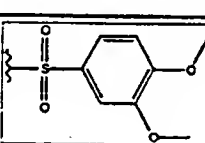
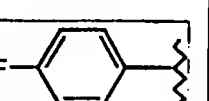
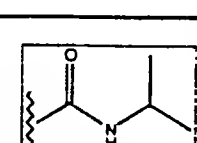
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0744			86	537	538
B-0745			82	482	483
B-0746			74	442	443
B-0747			83	444	445
B-0748			94	430	431
B-0749			100	455	456
B-0750			100	455	456
B-0751			48	444	445

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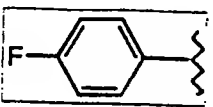
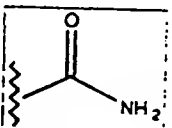
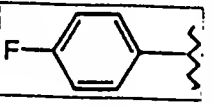
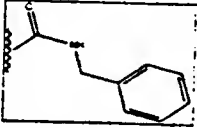
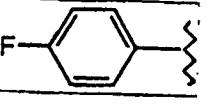
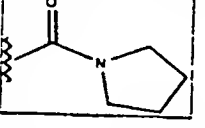
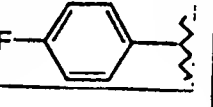
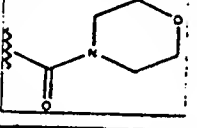
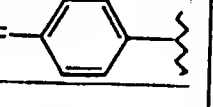
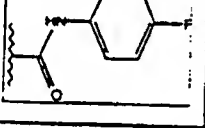
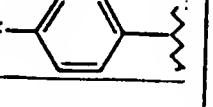
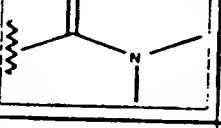
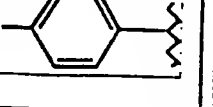
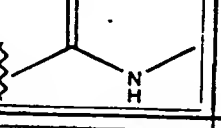
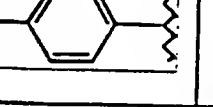

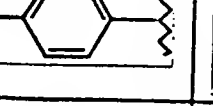
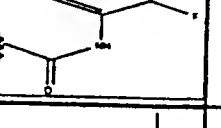
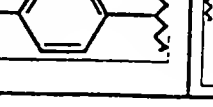
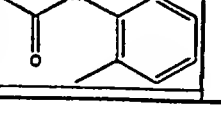


Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0752			84	516	517
B-0753			67	498	499
B-0754			31	464	465
B-0755			85	524	525
B-0756			77	512	513
B-0757			57	534	535
B-0758			36	490	491

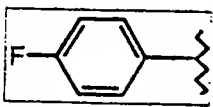
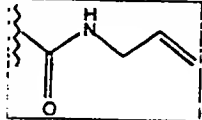
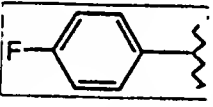
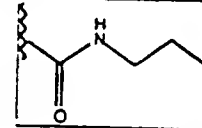
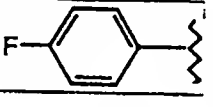
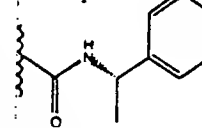
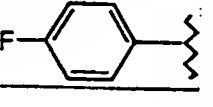
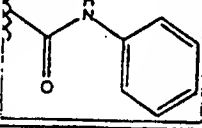
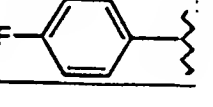

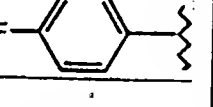
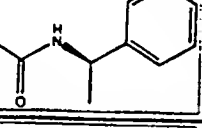
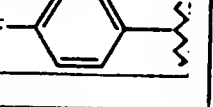
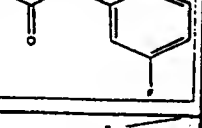
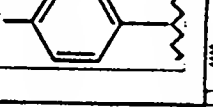

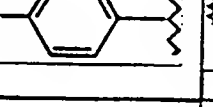
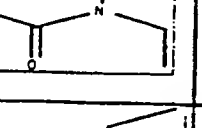
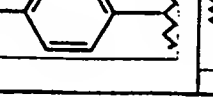
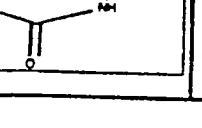
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Example#	R <sup>2</sup>	R <sup>J</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0759			79	516	517
B-0760			53	464	465
B-0761			50	478	479
B-0762			60	450	451
B-0763			75	436	437
B-0764			43	528	529
B-0765			75	504	505
B-0766			67	512	513
B-0767			43	558	559
B-0768			78	443	444

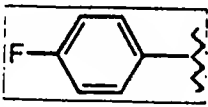
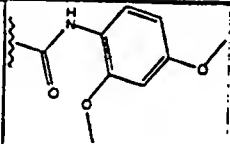
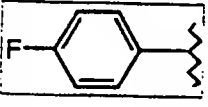
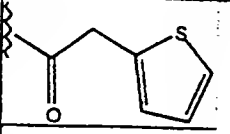
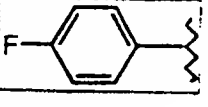
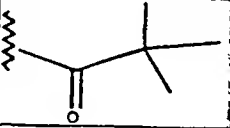
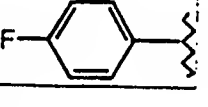
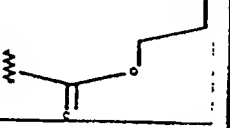
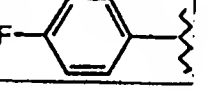
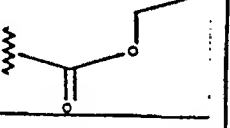
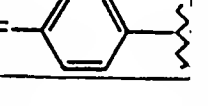
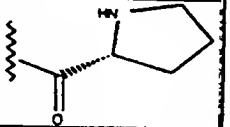
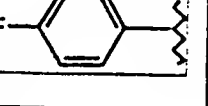
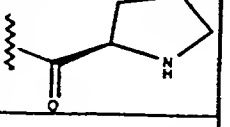
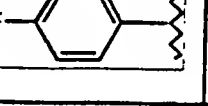
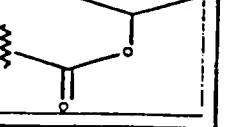
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Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0769			76	401	402
B-0770			57	491	492
B-0771			14	455	456
B-0772			72	471	472
B-0773			100	495	496
B-0774			41	429	430
B-0775			91	415	416
B-0776			64	491	492
B-0777			90	495	496
B-0778			19	505	506

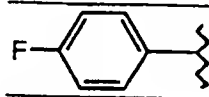
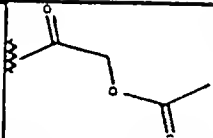
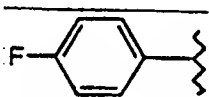
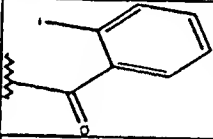
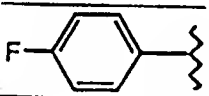
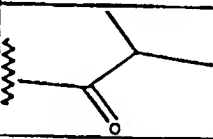
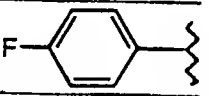
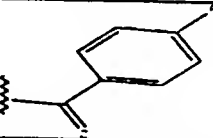
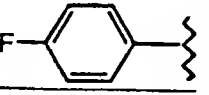
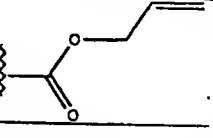
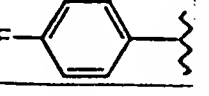
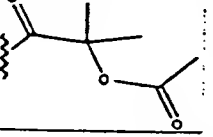
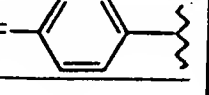
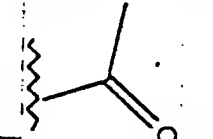
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Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0779			79	441	442
B-0780			40	443	444
B-0781			93	505	506
B-0782			57	477	478
B-0783			99	505	506
B-0784			100	505	506
B-0785			92	495	496
B-0786			91	507	508
B-0787			15	457	458
B-0788			48	429	430

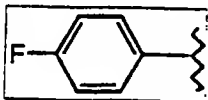
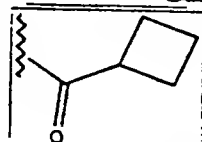
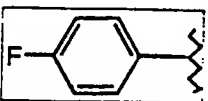
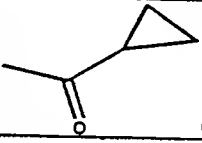
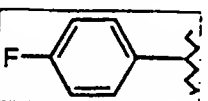
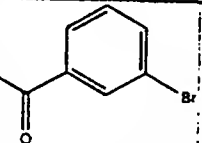
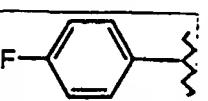
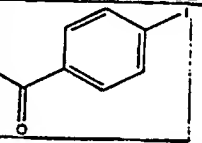
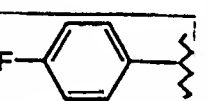
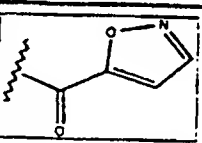
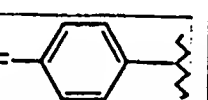
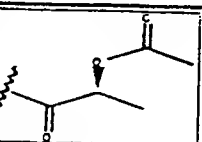
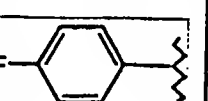
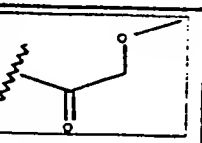
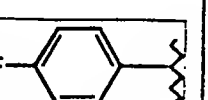
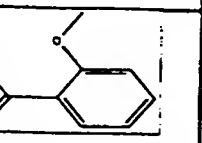
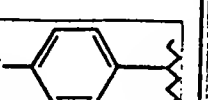
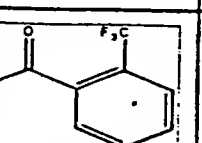
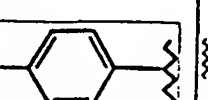
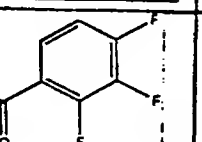
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Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0789			91	537	538
B-0790			93	482	483
B-0791			76	442	443
B-0792			96	444	445
B-0793			54	430	431
B-0794			100	455	456
B-0795			100	455	456
B-0796			94	444	445


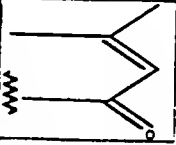
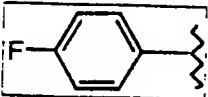
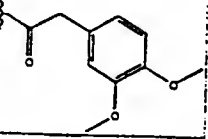
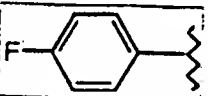
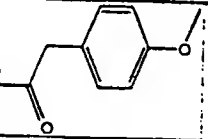
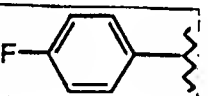
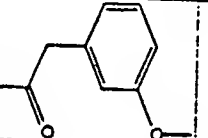
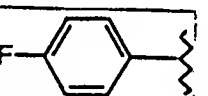
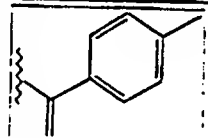
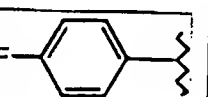
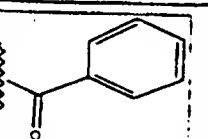
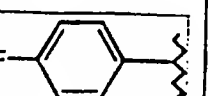
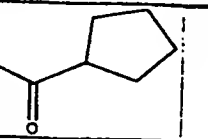
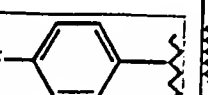
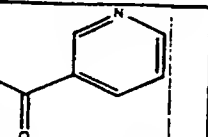
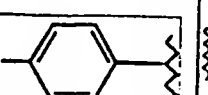
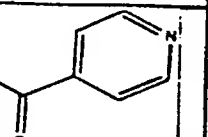
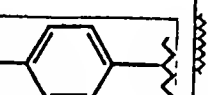
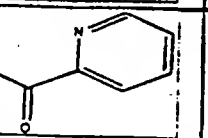
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Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0797			90	458	459
B-0798			90	588	589
B-0799			82	428	429
B-0800			92	480	481
B-0801			82	442	443
B-0802			95	486	487
B-0803			89	400	401

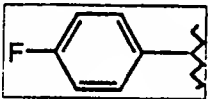
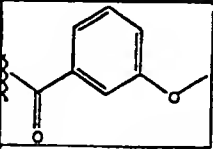
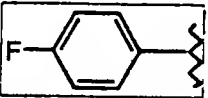
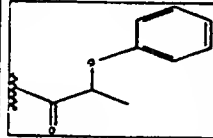
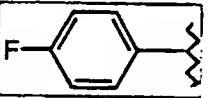
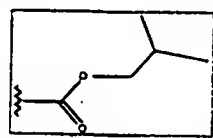
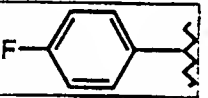
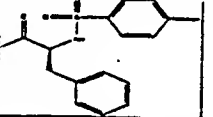
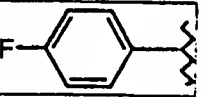
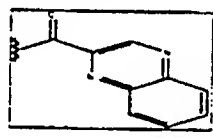
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Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0804			87	440	441
B-0805			100	426	427
B-0806			99	540	541
B-0807			96	588	589
B-0808			82	453	454
B-0809			92	472	473
B-0810			98	430	431
B-0811			88	492	493
B-0812			81	530	531
B-0813			98	516	517

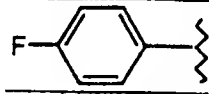
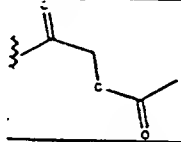
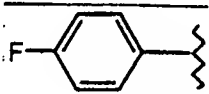
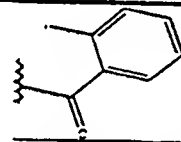
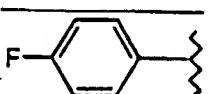
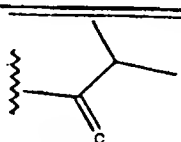
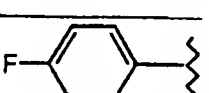
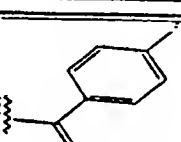
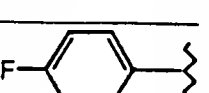
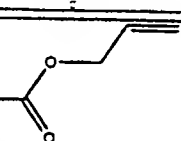
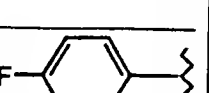
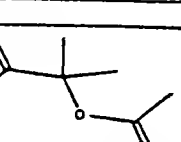
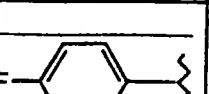
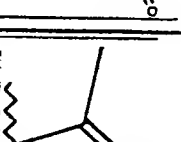
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Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0814			100	440	441
B-0815			100	536	537
B-0816			99	506	507
B-0817			98	506	507
B-0818			86	476	477
B-0819			90	462	463
B-0820			91	454	455
B-0821			69	463	464
B-0822			79	463	464
B-0823			79	463	464

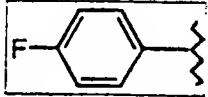
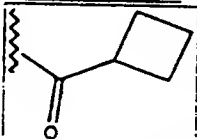
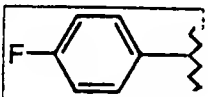
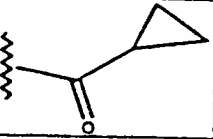
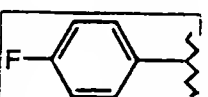
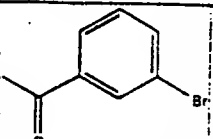
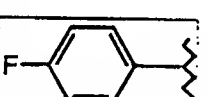
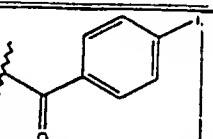
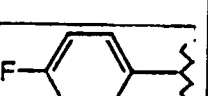
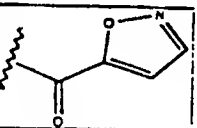
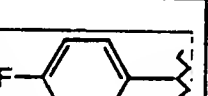
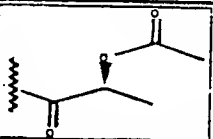
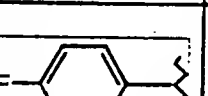
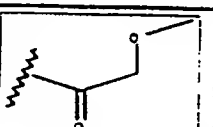
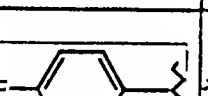
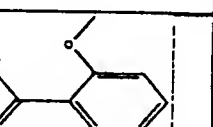

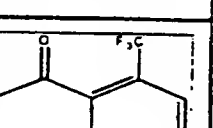

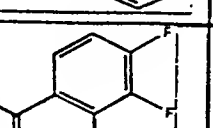
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Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0824			82	492	493
B-0825			100	506	507
B-0826			97	458	459
B-0827			100	659	660
B-0828			97	514	515

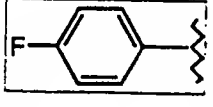
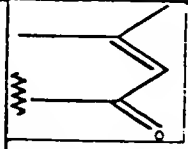
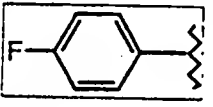
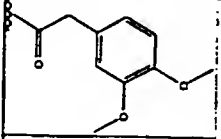
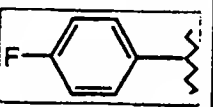
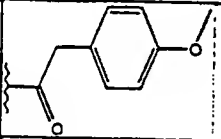
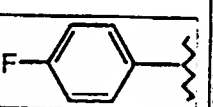
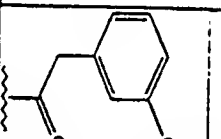
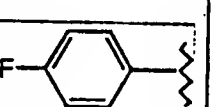
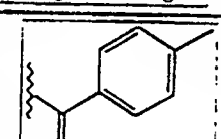
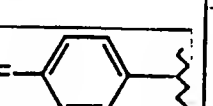
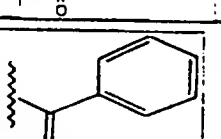
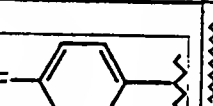
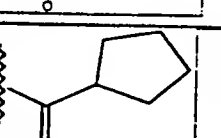
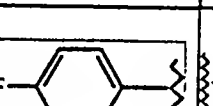
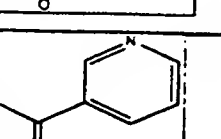
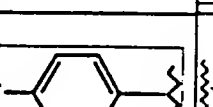
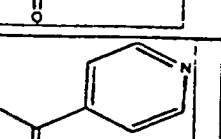
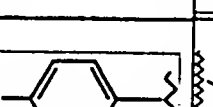
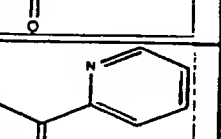
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Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0829			63	458	459
B-830			70	588	589
B-0831			100	428	429
B-0832			81	480	481
B-0833			73	442	443
B-0834			79	486	487
B-0835			5	400	401

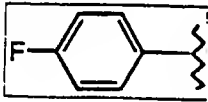
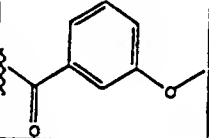
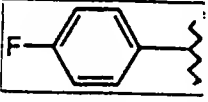
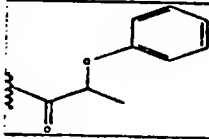
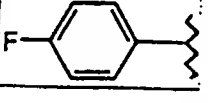
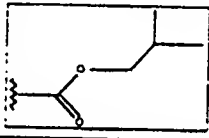
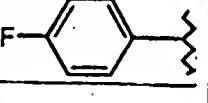
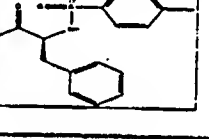
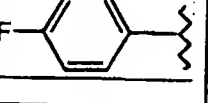
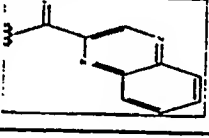
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Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0836			28	440	441
B-0837			81	426	427
B-0838			84	540	541
B-0839			80	588	589
B-0840			71	453	454
B-0841			55	472	473
B-0842			71	430	431
B-0843			68	492	493
B-0844			61	530	531
B-0845			84	516	517

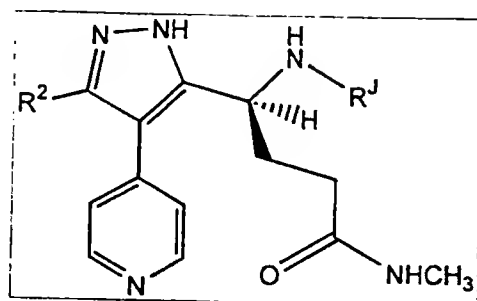
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Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0846			87	440	441
B-0847			86	536	537
B-0848			79	506	507
B-0849			81	506	507
B-0850			69	476	477
B-0851			83	462	463
B-0852			77	454	455
B-0853			87	463	464
B-0854			73	463	464
B-0855			92	463	464

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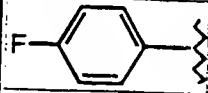
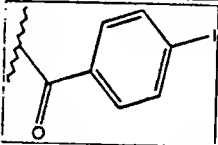
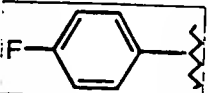
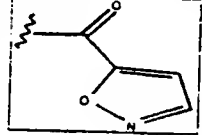
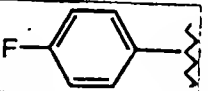
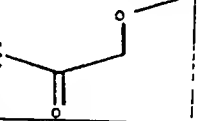
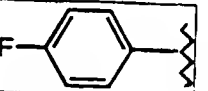
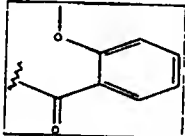
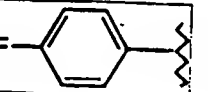
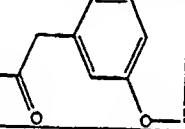
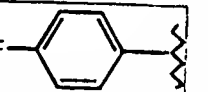
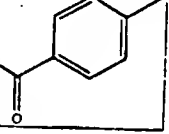
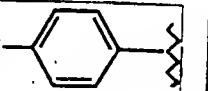
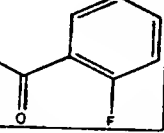
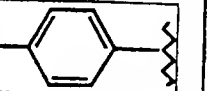
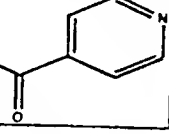
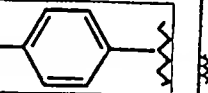
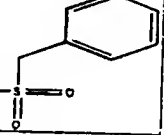
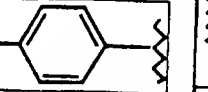
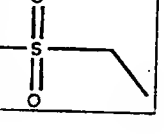
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0856			75	492	493
B-0857			86	506	507
B-0858			84	458	459
B-0859			80	659	660
B-0860			94	514	515

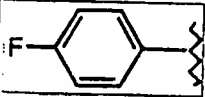
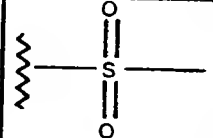
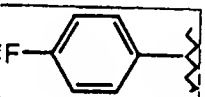
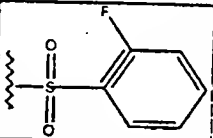
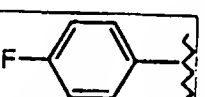
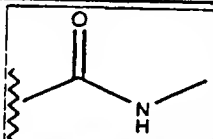
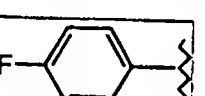
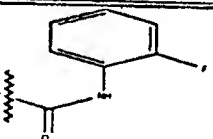
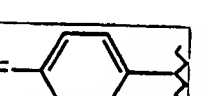
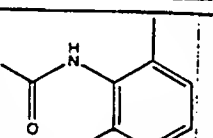
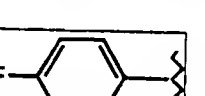
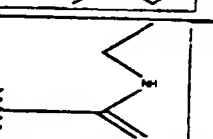
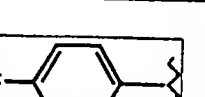
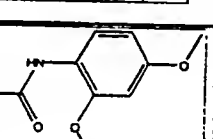
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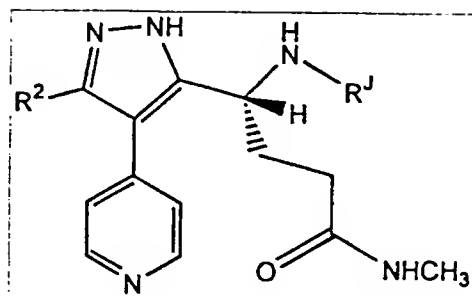
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0861			84	583	584
B-0862			96	475	476
B-0863			69	423	424
B-0864			86	437	438
B-0865			62	395	-
B-0866			81	421	422
B-0867			100	535	536

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Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0868			89	583	584
B-0869			100	448	449
B-0870			100	425	426
B-0871			100	487	488
B-0872			78	501	502
B-0873			78	471	472
B-0874			92	475	476
B-0875			37	458	459
B-0876			69	507	508
B-0877			70	445	446

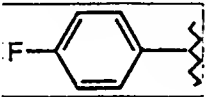
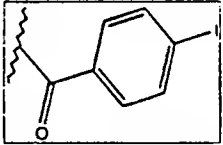
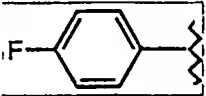
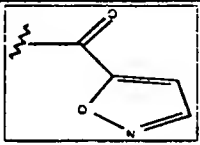
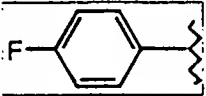
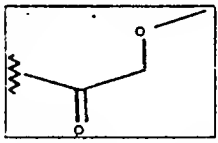
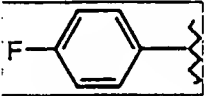
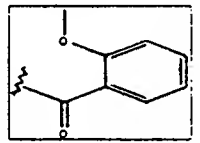
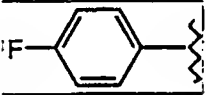
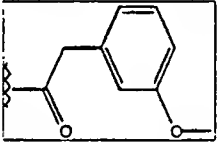
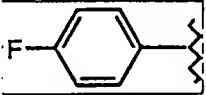
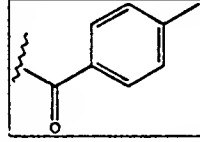
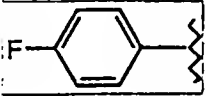
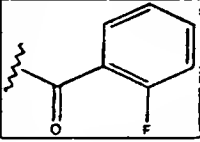
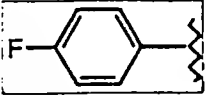
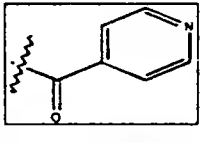
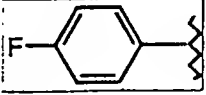
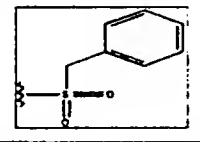
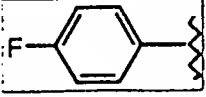
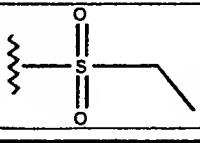
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0878			91	431	432
B-0879			92	511	512
B-0880			89	410	411
B-0881			84	490	491
B-0882			85	500	501
B-0883			85	424	425
B-0884			86	532	533

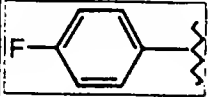
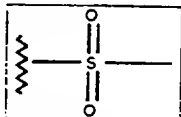
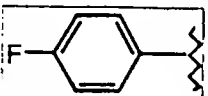
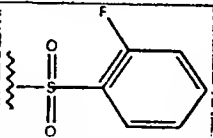
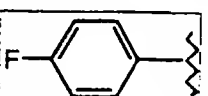
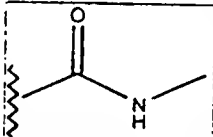
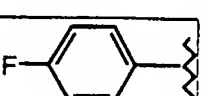
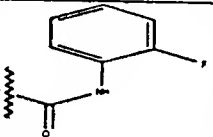
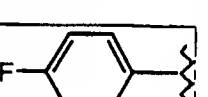
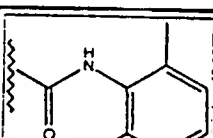
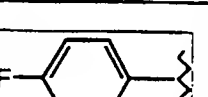
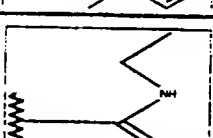
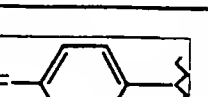
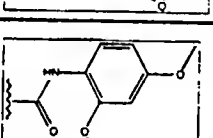
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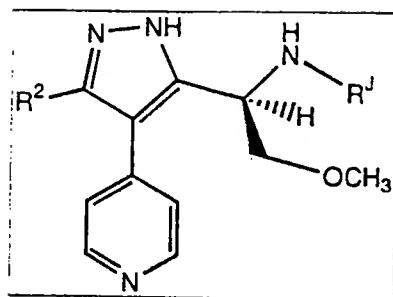
Example#	R <sup>2</sup>	R <sup>J</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0885			51	583	-
B-0886			97	475	-
B-0887			29	423	424
B-0888			82	437	438
B-0889			93	395	396
B-0890			91	421	422
B-0891			43	535	536

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Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0892			62	583	584
B-0893			95	448	449
B-0894			100	425	426
B-0895			76	487	488
B-0896			62	501	502
B-0897			80	471	472
B-0898			79	475	476
B-0899			70	458	459
B-0900			62	507	508
B-0901			43	445	446

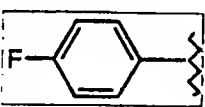
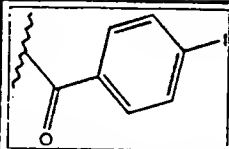
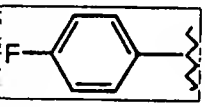
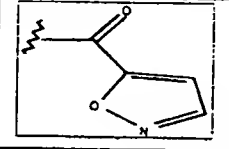
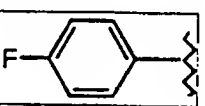
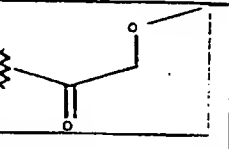
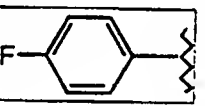
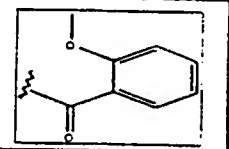
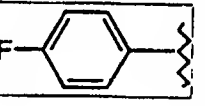
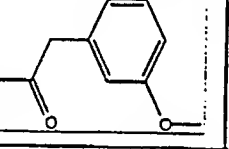
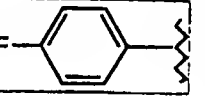
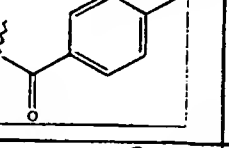
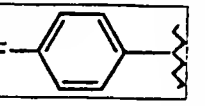
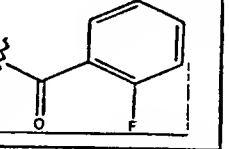
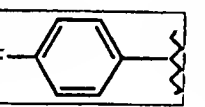
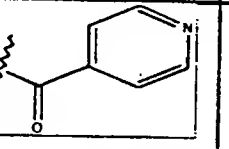
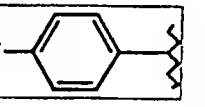
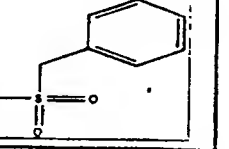
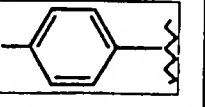
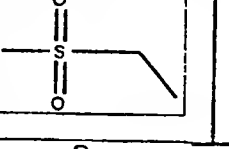
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0902			93	431	432
B-0903			100	511	512
B-0904			95	410	411
B-0905			89	490	491
B-0906			69	500	501
B-0907			28	424	425
B-0908			64	532	533

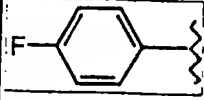
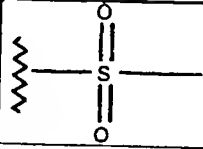
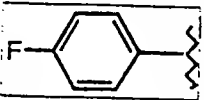
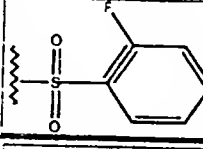
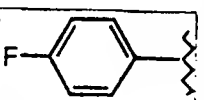
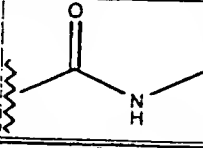
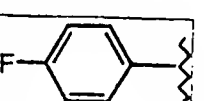
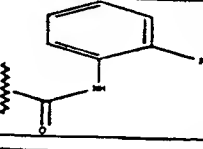
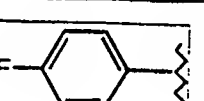
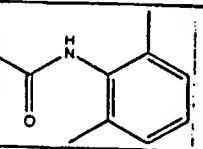
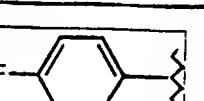
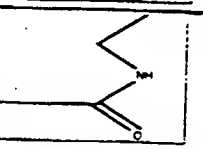
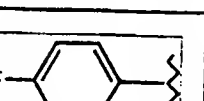
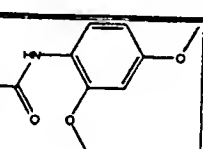
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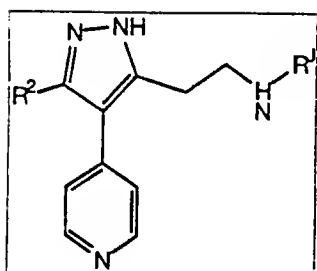
Example#	R <sup>2</sup>	R <sup>J</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0909			83	542	543
B-0910			80	434	435
B-0911			91	382	383
B-0912			100	396	397
B-0913			94	354	355
B-0914			95	380	381
B-0915			98	494	495

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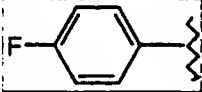
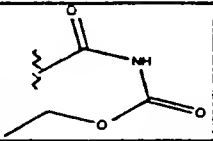
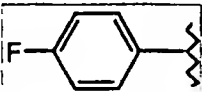
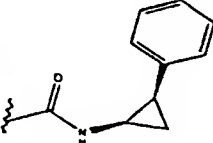
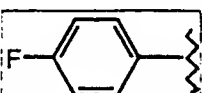
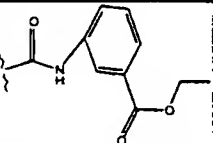
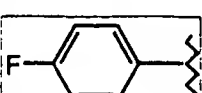
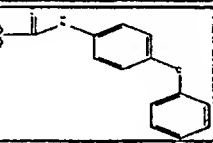
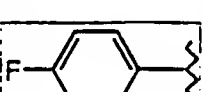
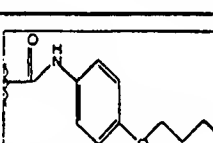
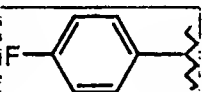
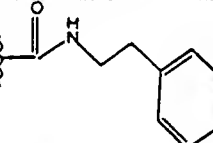
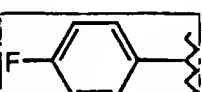
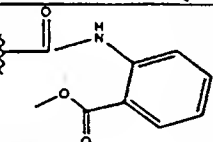
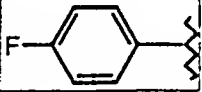
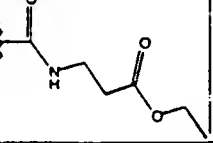
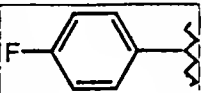
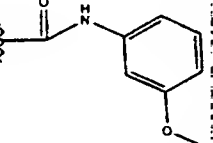
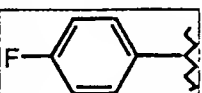
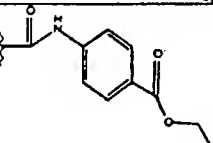
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0916			84	542	543
B-0917			79	407	408
B-0918			89	384	385
B-0919			91	446	447
B-0920			99	460	461
B-0921			84	430	431
B-0922			81	434	435
B-0923			76	417	418
B-0924			70	466	467
B-0925			64	404	405

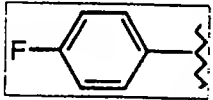
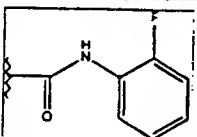
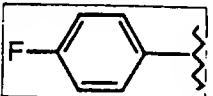
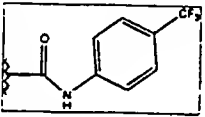
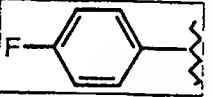
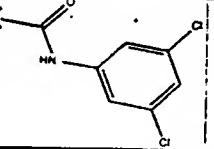
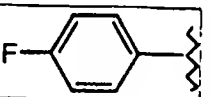
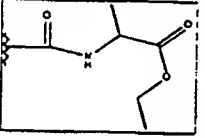
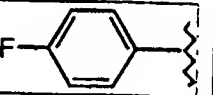
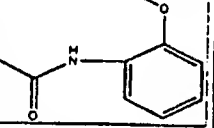
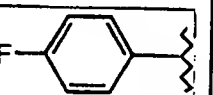
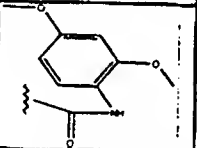
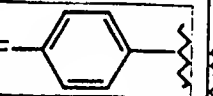
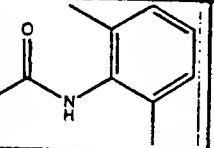
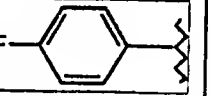
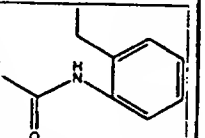
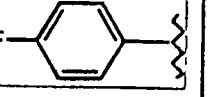
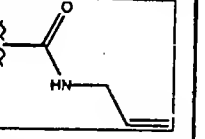
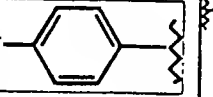
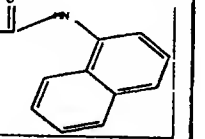
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0926			47	390	391
B-0927			89	470	471
B-0928			53	369	370
B-0929			100	449	450
B-0930			14	459	460
B-0931			41	383	384
B-0932			94	491	492

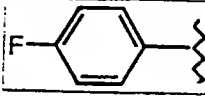
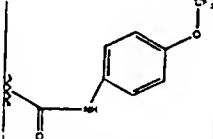
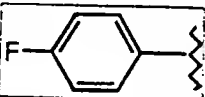
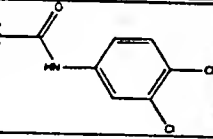
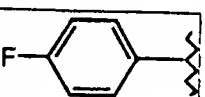
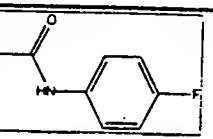
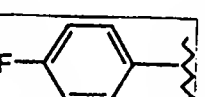
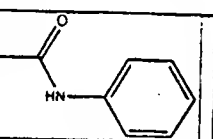
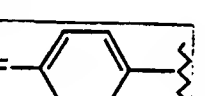
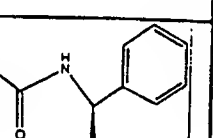
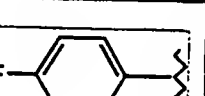
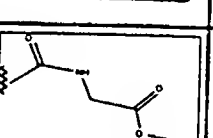
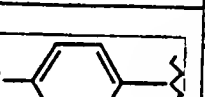
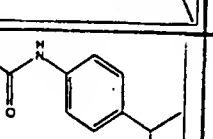
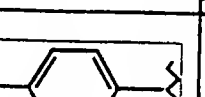
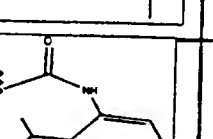
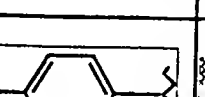
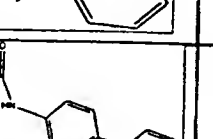
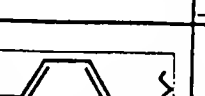
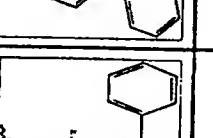
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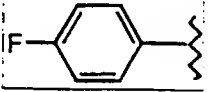
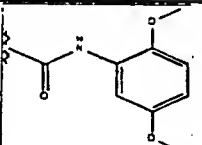
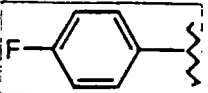
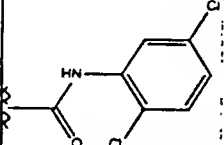
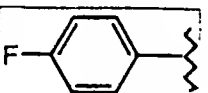
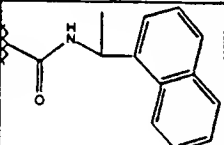
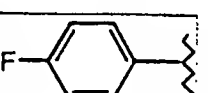
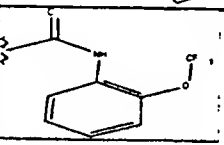
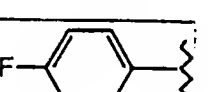
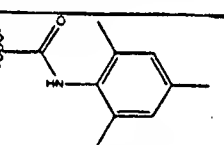
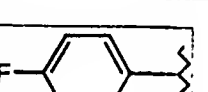
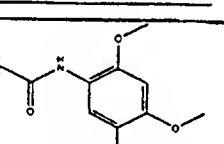
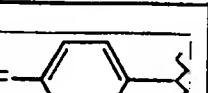
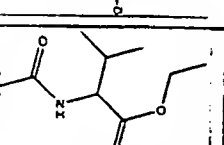
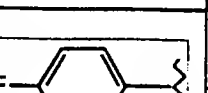
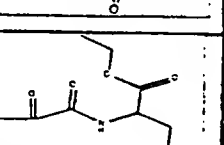

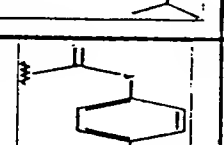

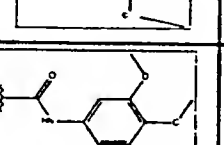


Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0933			48	447	448
B-0934			44	429	430
B-0935			33	485	486
B-0936			30	479	-
B-0937			68	367	368
B-0938			72	479	480
B-0939			76	415	416

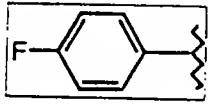
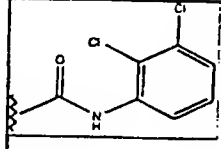
Example#	R <sup>2</sup>	R <sup>J</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0940			36	397	398
B-0941			41	441	442
B-0942			27	473	474
B-0943			55	493	494
B-0944			53	473	474
B-0945			82	429	430
B-0946			100	459	460
B-0947			60	425	426
B-0948			100	431	432
B-0949			98	473	474

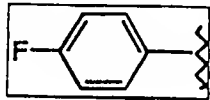
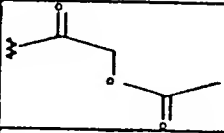
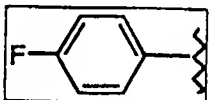
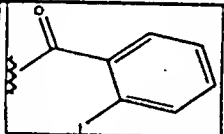
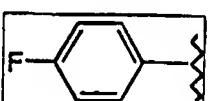
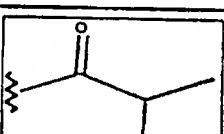
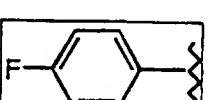
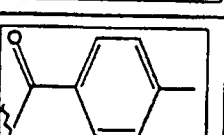
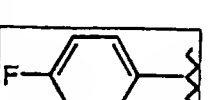
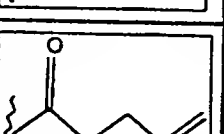
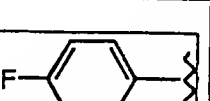
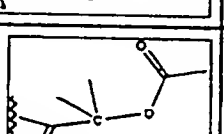
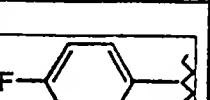
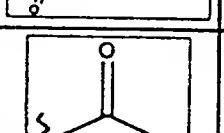
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0950			64	419	420
B-0951			100	469	470
B-0952			61	469	470
B-0953			67	425	426
B-0954			62	431	432
B-0955			39	461	462
B-0956			66	429	430
B-0957			93	429	430
B-0958			86	365	366
B-0959			73	451	452

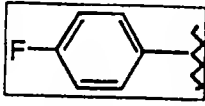
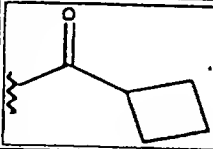
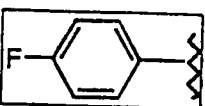
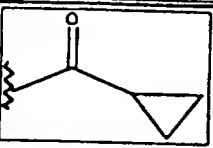
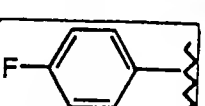
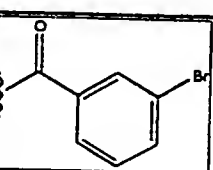
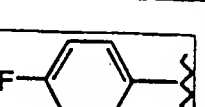
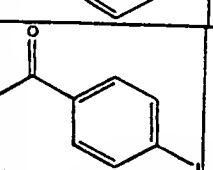
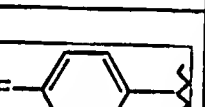
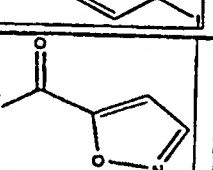
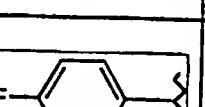
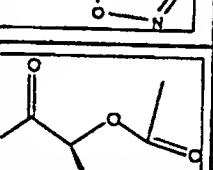

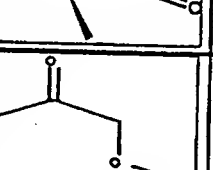

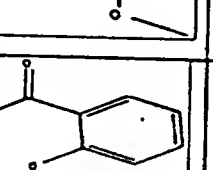

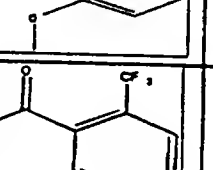
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0960			98	485	486
B-0961			100	469	470
B-0962			100	419	420
B-0963			83	401	402
B-0964			38	429	430
B-0965			90	411	412
B-0966			76	443	444
B-0967			100	443	444
B-0968			100	477	478
B-0969			77	477	478

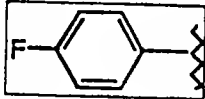
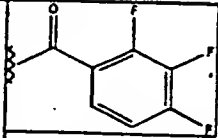
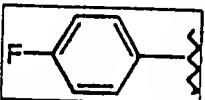
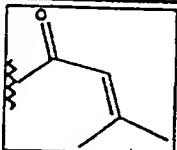
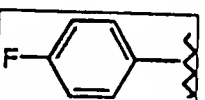
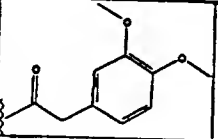
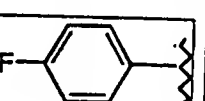
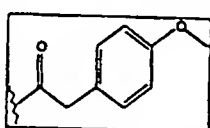
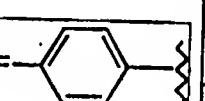
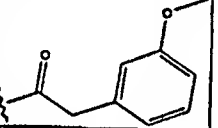
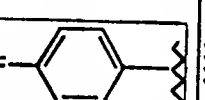
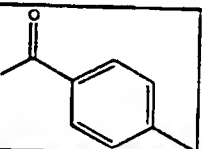
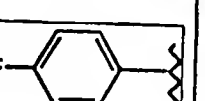
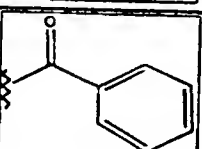
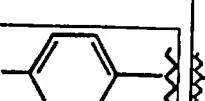
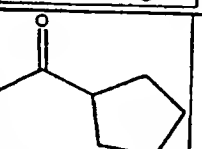
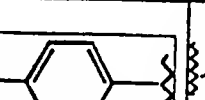
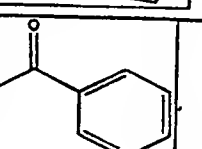
Example#	R <sup>2</sup>	R <sup>J</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0970			38	461	462
B-0971			95	469	470
B-0972			98	479	480
B-0973			96	485	486
B-0974			74	443	444
B-0975			100	495	496
B-0976			70	453	454
B-0977			100	467	468
B-0978			91	431	432
B-0979			54	491	492

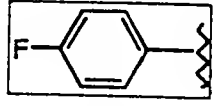
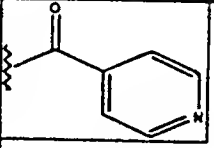
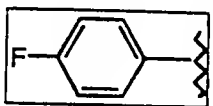
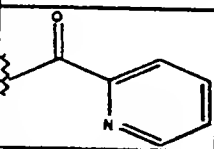
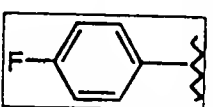
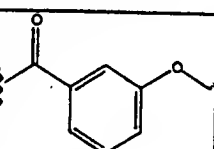
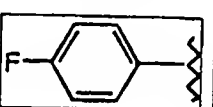
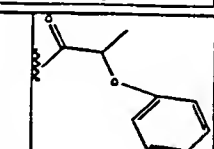
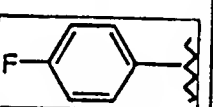
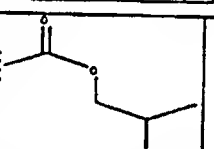
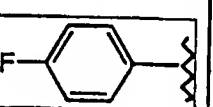
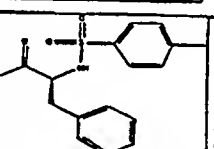
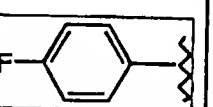
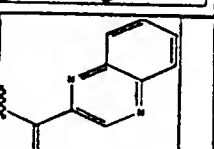
700

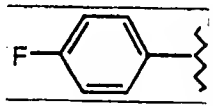
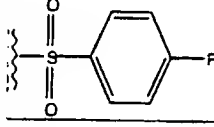
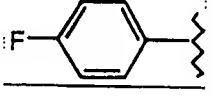
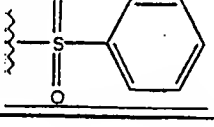
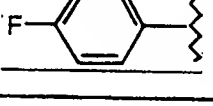
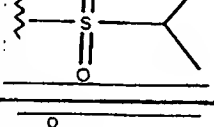
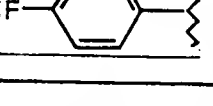
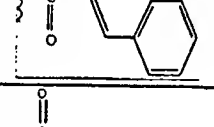

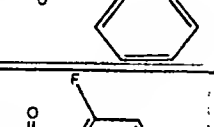
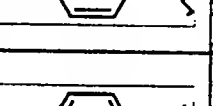
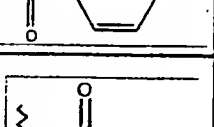

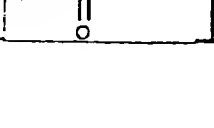
Example#	R <sup>2</sup>	R <sup>J</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0980			65	469	470

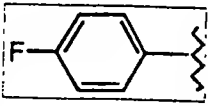
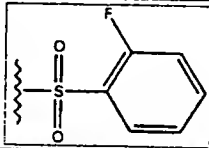
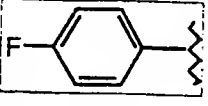
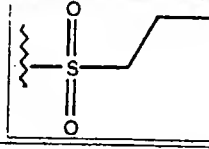
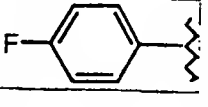
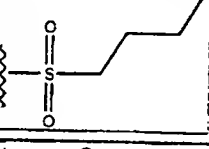
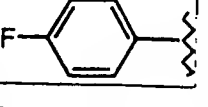
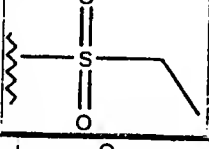
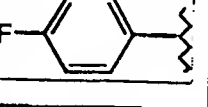
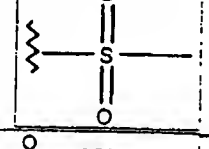
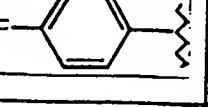
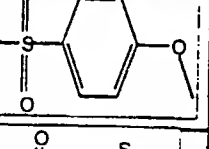
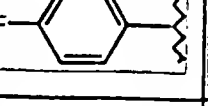
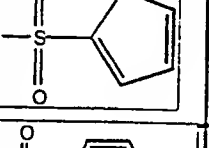
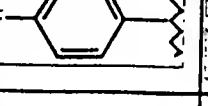
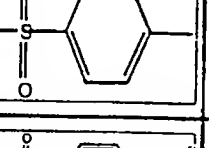
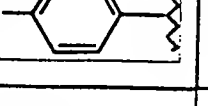
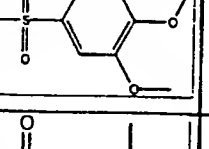
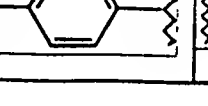
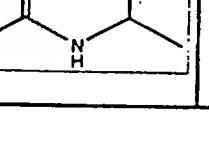
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0981			78	382	383
B-0982			82	512	513
B-0983			94	352	353
B-0984			81	404	405
B-0985			84	366	367
B-0986			80	410	411
B-0987			85	324	325

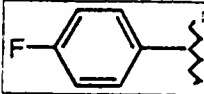
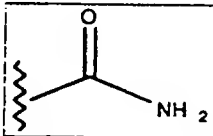
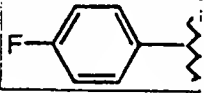
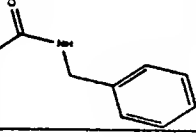
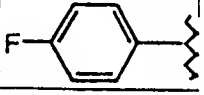
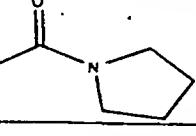
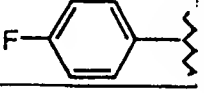
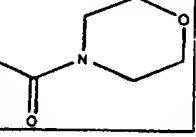
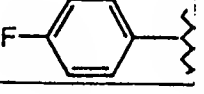
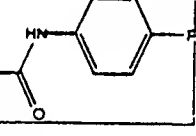
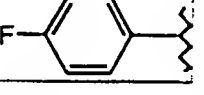
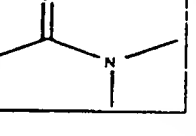
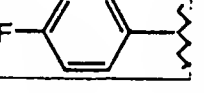
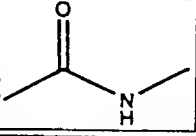
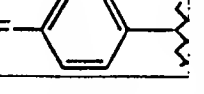
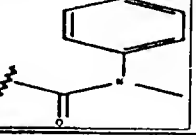
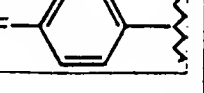
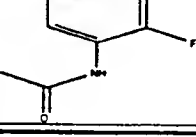
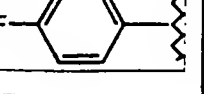
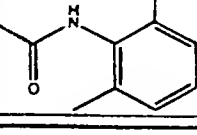
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0988			91	364	365
B-0989			88	350	351
B-0990			68	464	465
B-0991			86	512	513
B-0992			79	377	378
B-0993			81	396	397
B-0994			100	354	355
B-0995			75	416	417
B-0996			65	454	455

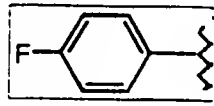
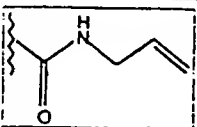
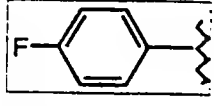
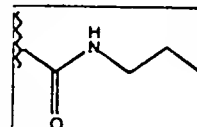
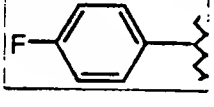
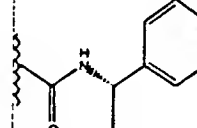
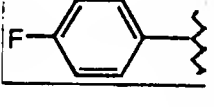
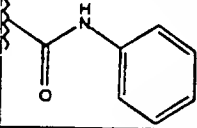
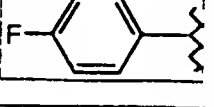

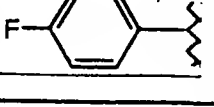
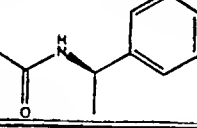
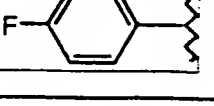
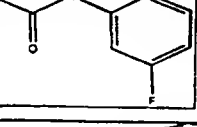
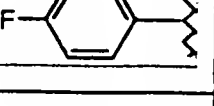

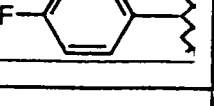
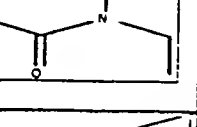
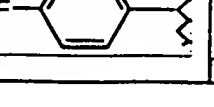
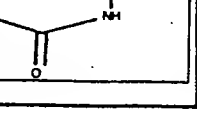
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-0997			64	440	441
B-0998			81	364	365
B-0999			79	460	461
B-1000			84	430	431
B-1001			78	430	431
B-1002			85	400	401
B-1003			83	386	387
B-1004			87	378	379
B-1005			57	387	388

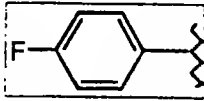
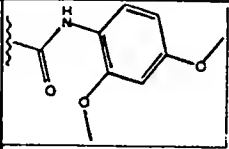
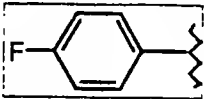
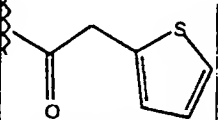
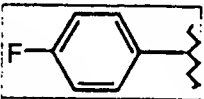
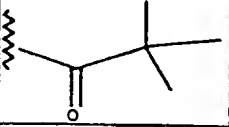
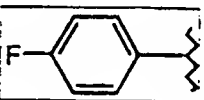
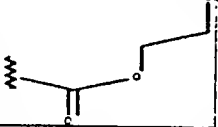
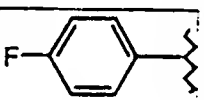
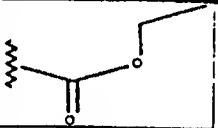
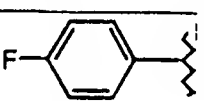
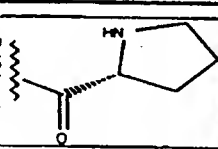
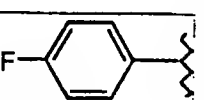
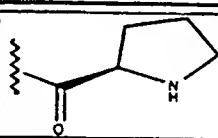
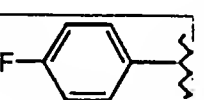
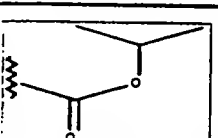
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1006			80	387	388
B-1007			54	387	388
B-1008			64	416	417
B-1009			81	430	431
B-1010			81	382	383
B-1011			66	583	584
B-1012			69	438	439

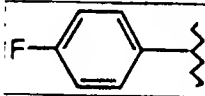
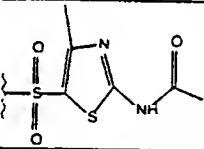
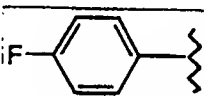
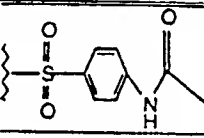
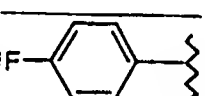
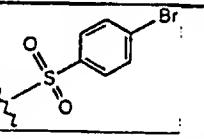
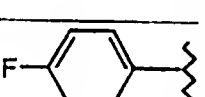
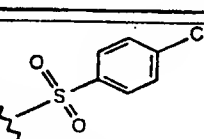
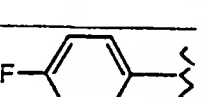
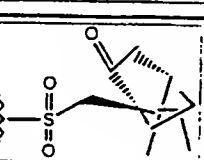
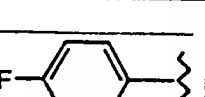
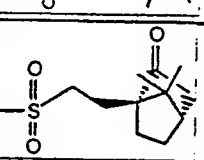
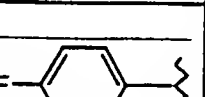
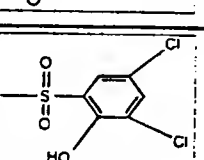
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1013			53	440	441
B-1014			61	422	423
B-1015			47	388	389
B-1016			74	448	449
B-1017			63	436	437
B-1018			82	458	459
B-1019			41	414	415

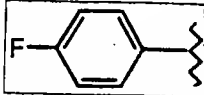
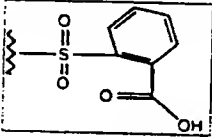
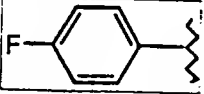
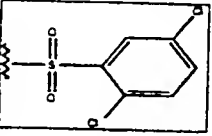
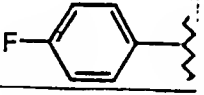
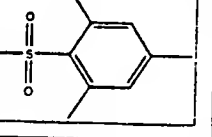
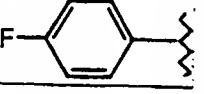
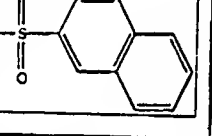
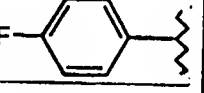

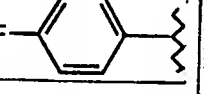
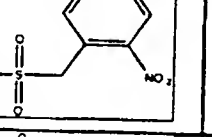
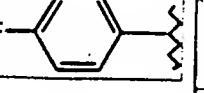

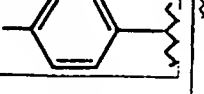
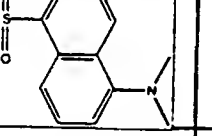
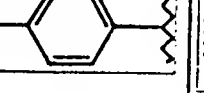
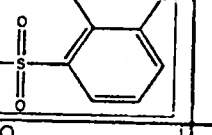
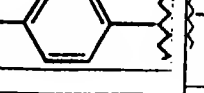

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1020			100	440	441
B-1021			100	388	389
B-1022			74	402	403
B-1023			76	374	375
B-1024			73	360	361
B-1025			100	452	453
B-1026			95	428	429
B-1027			98	436	437
B-1028			100	482	483
B-1029			98	367	368

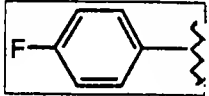
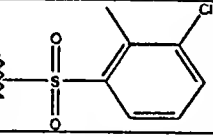
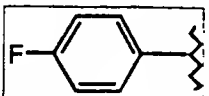
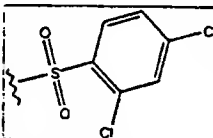
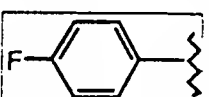
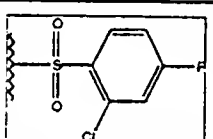
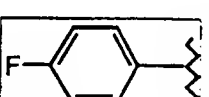
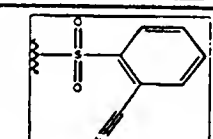
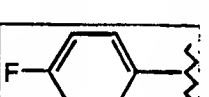
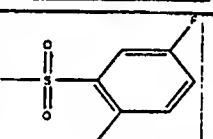
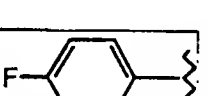
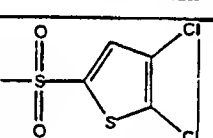
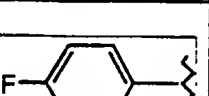
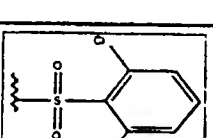
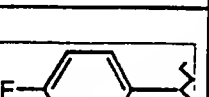
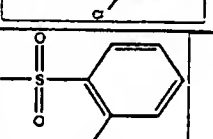

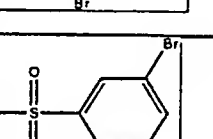

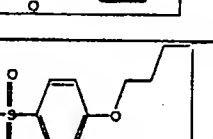
Example#	R <sup>2</sup>	R <sup>J</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1030			88	325	326
B-1031			97	415	416
B-1032			64	379	380
B-1033			83	395	396
B-1034			67	419	420
B-1035			73	353	354
B-1036			79	339	340
B-1037			78	415	416
B-1038			100	419	420
B-1039			95	429	430

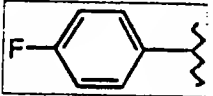
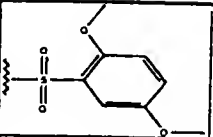
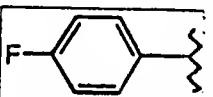
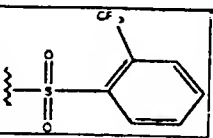
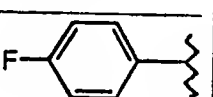
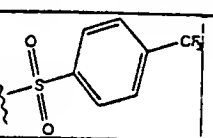
Example#	R <sup>2</sup>	R <sup>J</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1040			91	365	366
B-1041			88	367	368
B-1042			78	429	430
B-1043			79	401	402
B-1044			93	429	430
B-1045			100	429	430
B-1046			94	419	420
B-1047			100	431	432
B-1048			58	381	382
B-1049			97	353	354

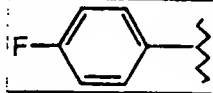
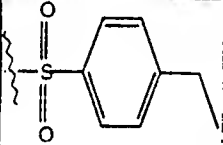
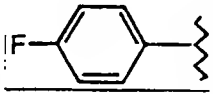
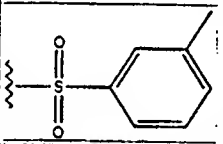
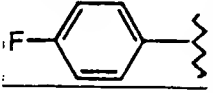
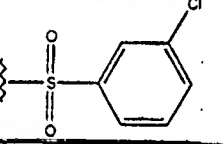
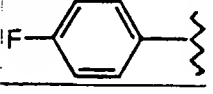
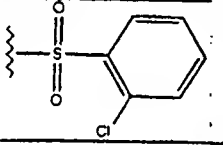
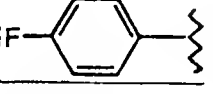
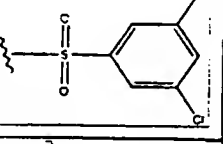
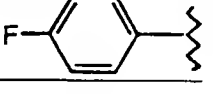
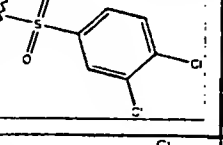
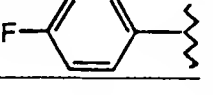
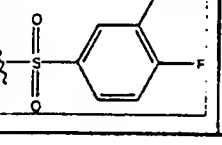
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1050			100	461	462
B-1051			88	406	407
B-1052			82	366	367
B-1053			21	368	
B-1054			98	354	355
B-1055			100	379	380
B-1056			85	379	380
B-1057			30	368	369

Example#	R <sup>2</sup>	R <sup>J</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1058			35	500	501
B-1059			77	479	480
B-1060			37	500	501
B-1061			86	456	457
B-1062			58	496	497
B-1063			59	496	497
B-1064			58	506	-

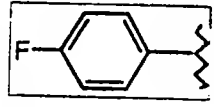
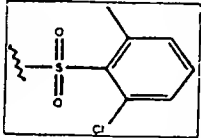
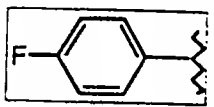
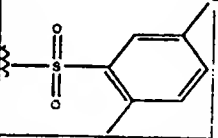
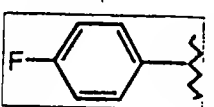
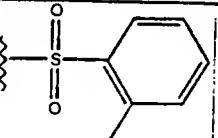
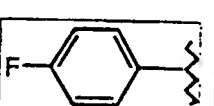
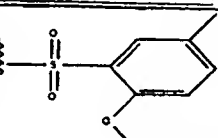
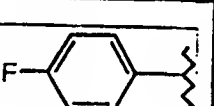
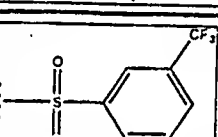
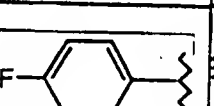
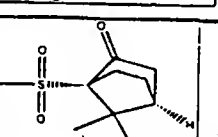
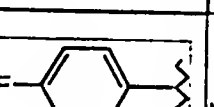
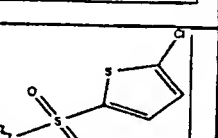
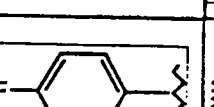
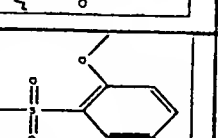
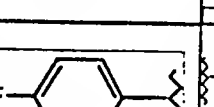
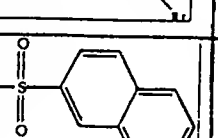
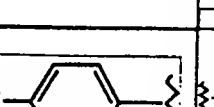
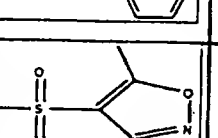
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1065			24	466	-
B-1066			100	490	491
B-1067			74	464	465
B-1068			79	472	473
B-1069			97	472	473
B-1070			54	481	482
B-1071			67	473	474
B-1072			35	515	516
B-1073			100	490	491
B-1074			100	464	465

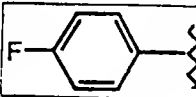
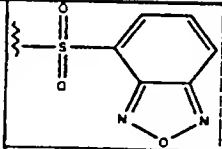
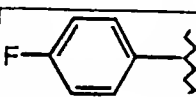
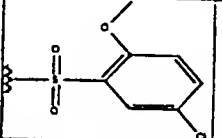
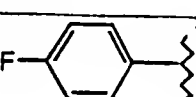
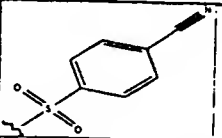
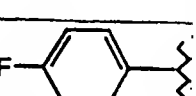
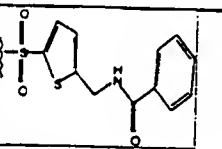
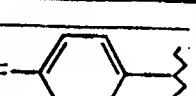
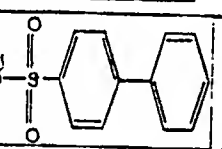
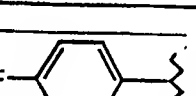
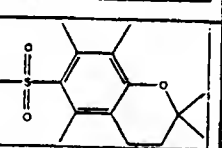
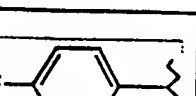
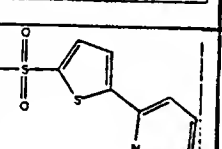
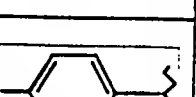
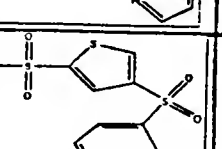

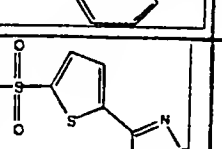
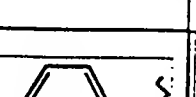
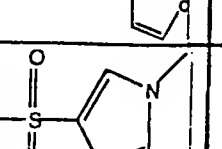
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1075			100	470	471
B-1076			93	490	491
B-1077			100	474	475
B-1078			80	447	448
B-1079			85	454	455
B-1080			100	496	497
B-1081			100	490	491
B-1082			100	500	501
B-1083			93	500	501
B-1084			81	494	495

Example#	R <sup>2</sup>	R <sup>3</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1085			93	482	483
B-1086			92	490	491
B-1087			100	490	491

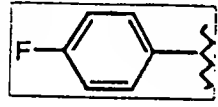
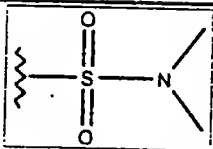
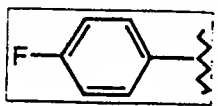
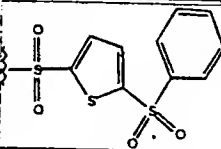
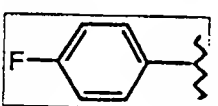
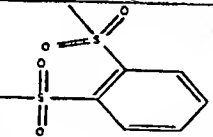
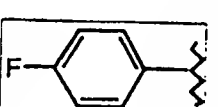
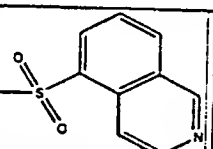
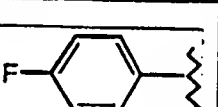
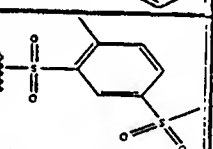
Example#	R <sup>2</sup>	R <sup>3</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1088			97	450	451
B-1089			100	436	437
B-1090			100	456	457
B-1091			100	456	457
B-1092			96	490	491
B-1093			100	490	491
B-1094			100	474	475

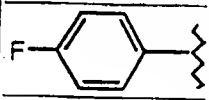
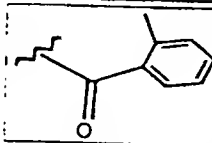
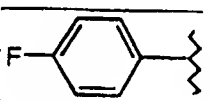
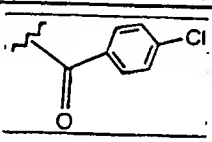
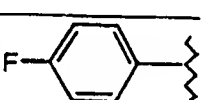
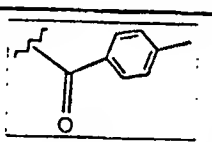
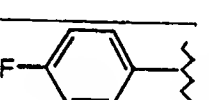
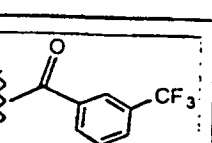
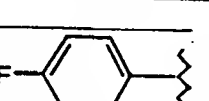
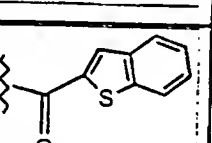
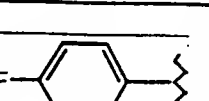
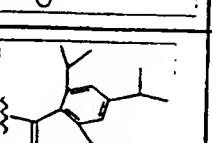
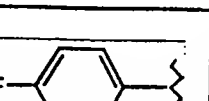
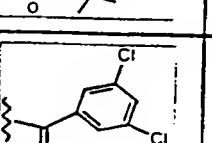
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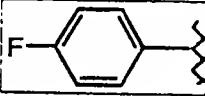
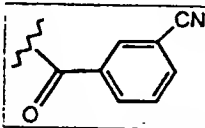
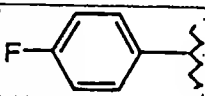
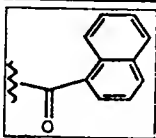
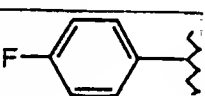
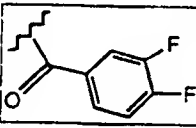
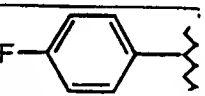
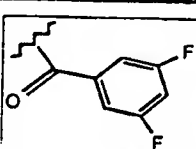
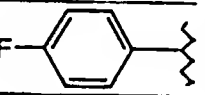
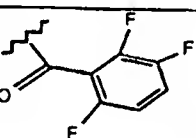
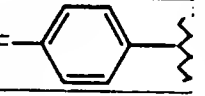
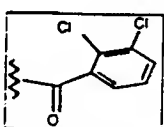
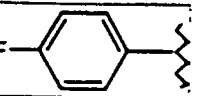
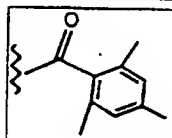
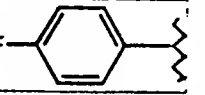
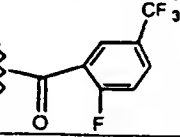
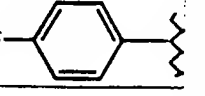
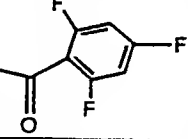
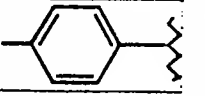
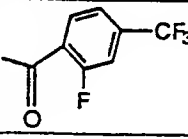
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1095			81	470	471
B-1096			77	450	451
B-1097			100	436	437
B-1098			93	466	467
B-1099			100	490	491
B-1100			47	482	-
B-1101			64	462	463
B-1102			98	530	531
B-1103			65	472	-
B-1104			88	441	442

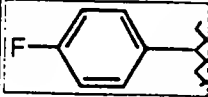
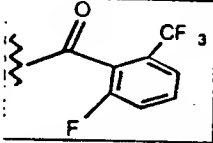
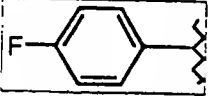
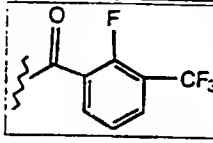
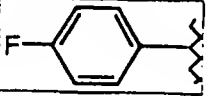
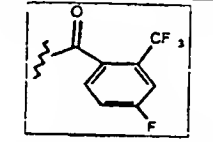
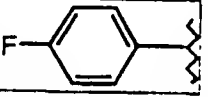
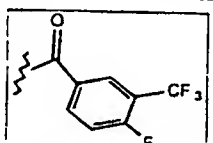
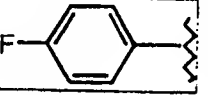
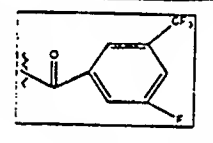
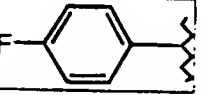
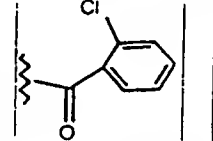
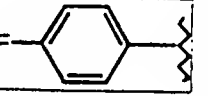
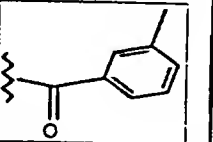
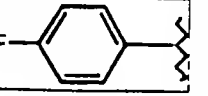
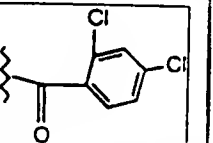
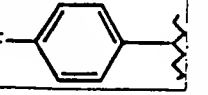
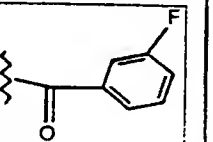
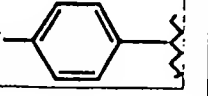
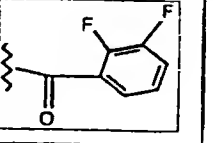
Example#	R <sup>2</sup>	R <sup>J</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1105			100	464	465
B-1106			91	486	487
B-1107			96	447	448
B-1108			55	561	562
B-1109			100	498	499
B-1110			73	548	549
B-1111			94	505	506
B-1112			100	568	569
B-1113			100	495	496
B-1114			73	426	427

717

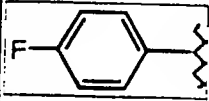
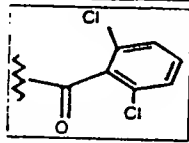
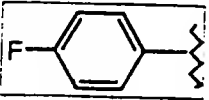
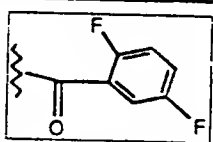
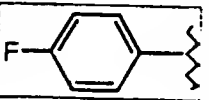
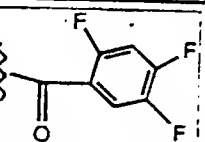
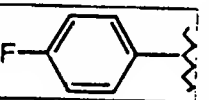
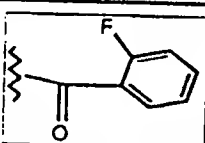
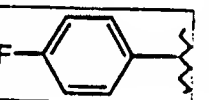
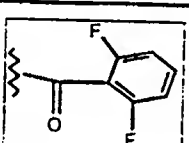
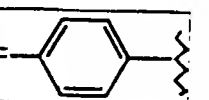
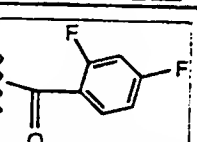
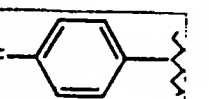
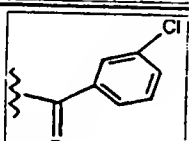
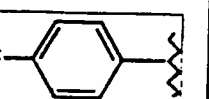
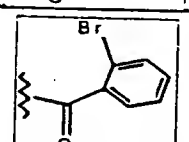
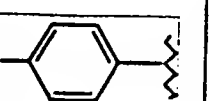
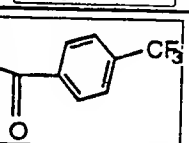
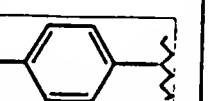
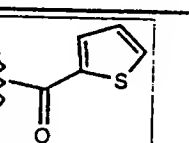
Example#	R <sup>2</sup>	R <sup>J</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1115			30	389	390
B-1116			100	568	569
B-1117			83	500	501
B-1118			55	473	-
B-1119			70	514	515

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1120			84	400	401
B-1121			86	420	421
B-1122			90	400	401
B-1123			100	454	455
B-1124			91	442	443
B-1125			50	512	513
B-1126			85	454	455

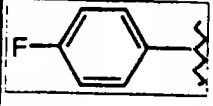
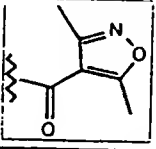
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1127			93	411	412
B-1128			87	436	437
B-1129			78	422	423
B-1130			96	422	423
B-1131			84	440	441
B-1132			77	454	455
B-1133			62	428	429
B-1134			91	472	473
B-1135			85	440	441
B-1136			82	472	473

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1137			95	472	473
B-1138			100	472	473
B-1139			100	472	473
B-1140			92	472	473
B-1141			100	472	473
B-1142			88	420	421
B-1143			90	400	401
B-1144			87	454	455
B-1145			93	404	405
B-1146			90	422	423

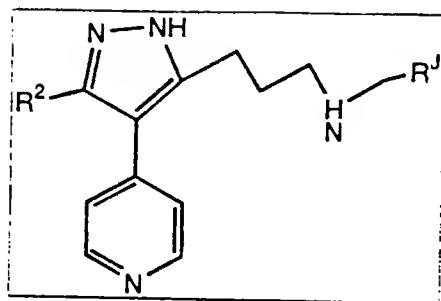
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Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1147			100	454	455
B-1148			87	422	423
B-1149			87	440	441
B-1150			90	404	405
B-1151			82	422	423
B-1152			85	422	423
B-1153			90	420	421
B-1154			78	464	465
B-1155			79	454	455
B-1156			95	392	393

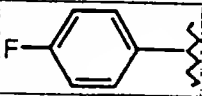
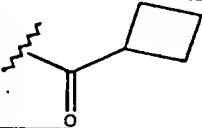
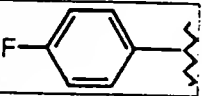
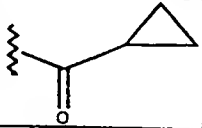
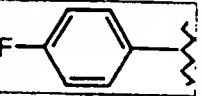
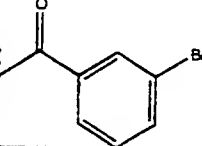
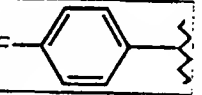
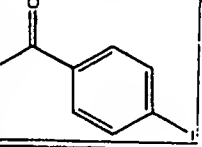
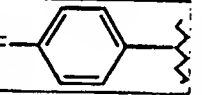
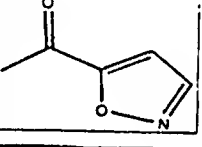
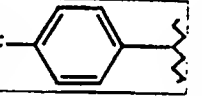
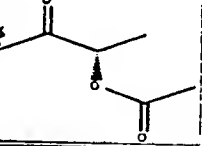
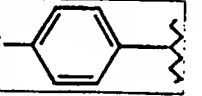
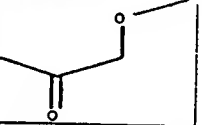
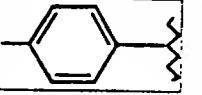
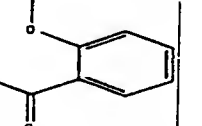
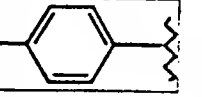
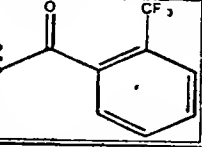
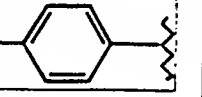
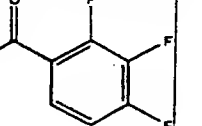
722

Example#	R <sup>2</sup>	R <sup>J</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1157			81	405	406

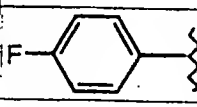
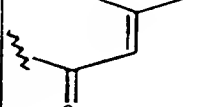
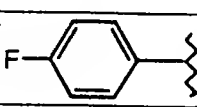
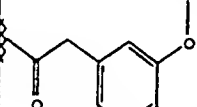
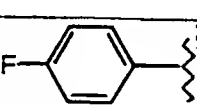
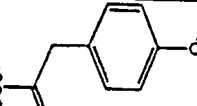
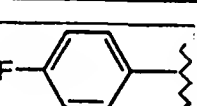
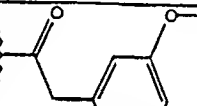
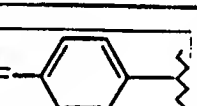
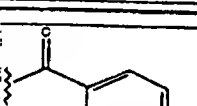
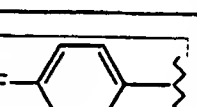
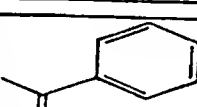
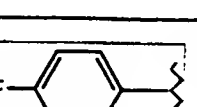
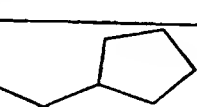
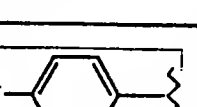
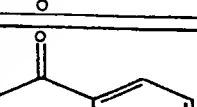
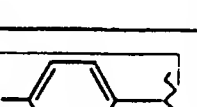
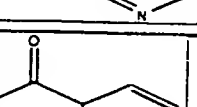

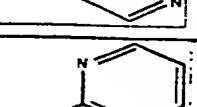
723

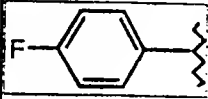
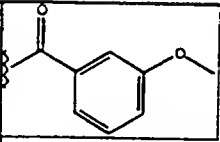
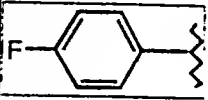
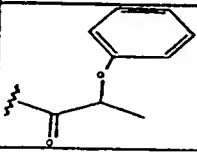
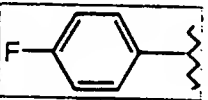
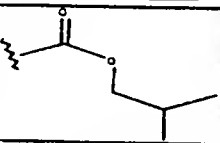
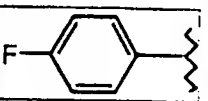
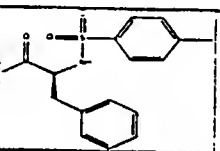
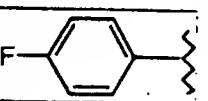
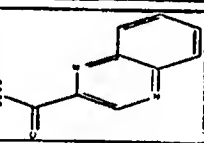


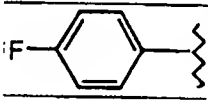
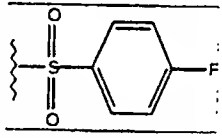
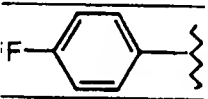
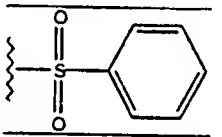
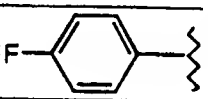
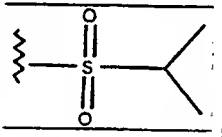
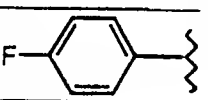
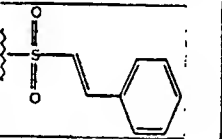
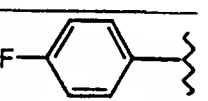
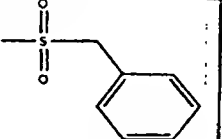
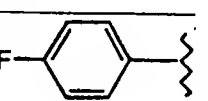
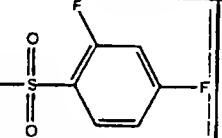
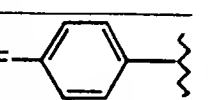
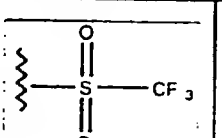
Example#	R <sup>2</sup>	R <sup>J</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1158			54	396	397
B-1159			42	526	527
B-1160			27	366	367
B-1161			58	418	419
B-1162			62	380	381
B-1163			58	424	425
B-1164			67	338	339

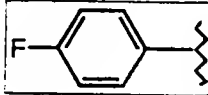
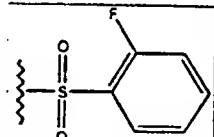
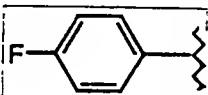
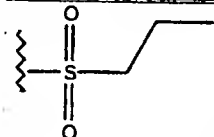
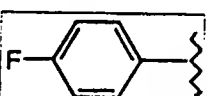
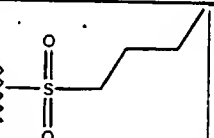
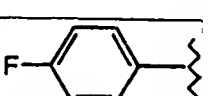
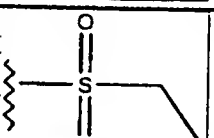
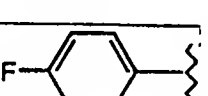
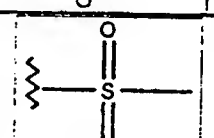
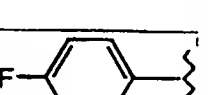
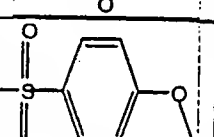
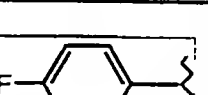
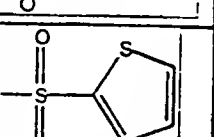
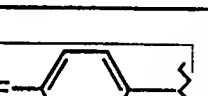
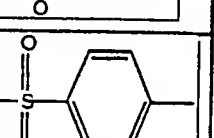

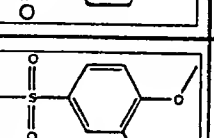

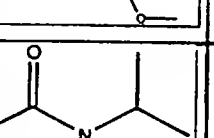
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1165			66	378	379
B-1166			65	364	365
B-1167			64	478	479
B-1168			76	526	527
B-1169			70	391	392
B-1170			76	410	411
B-1171			82	368	369
B-1172			73	430	431
B-1173			74	468	469
B-1174			83	454	455

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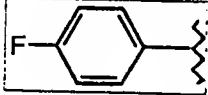
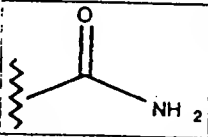
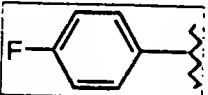
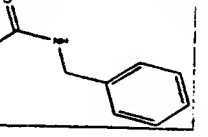
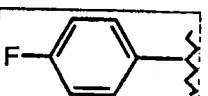
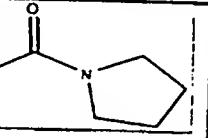
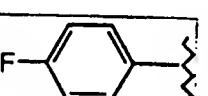
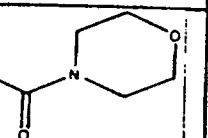
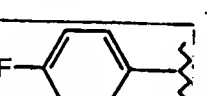
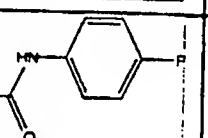
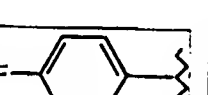
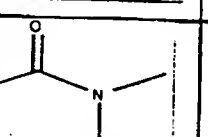
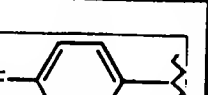
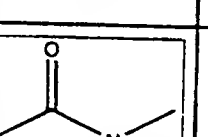
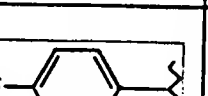
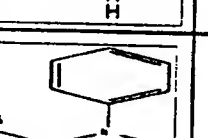

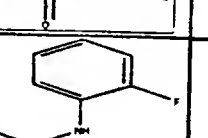

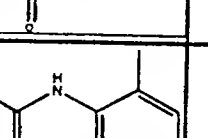
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1175			76	378	379
B-1176			96	474	475
B-1177			94	444	445
B-1178			90	444	445
B-1179			57	414	415
B-1180			75	400	401
B-1181			66	392	393
B-1182			74	401	402
B-1183			62	401	402
B-1184			51	401	402

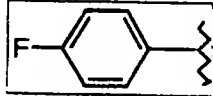
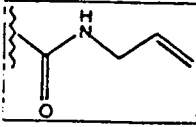
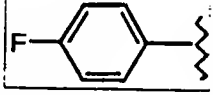
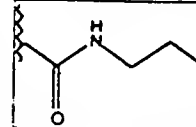
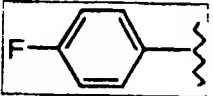
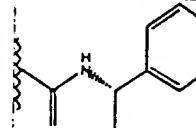
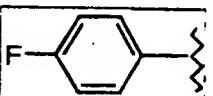
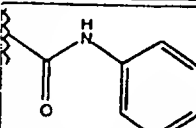
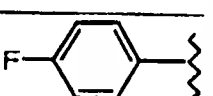

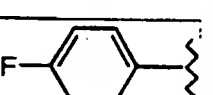
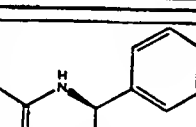
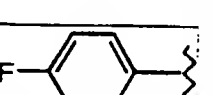
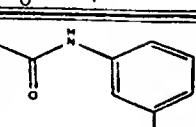
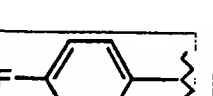
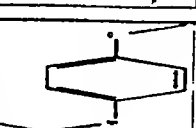
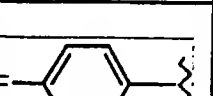
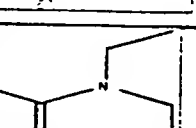
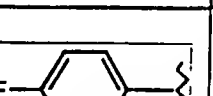
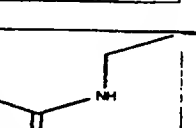
Example#	R <sup>2</sup>	R <sup>3</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1185			90	430	431
B-1186			86	444	445
B-1187			74	396	397
B-1188			76	597	598
B-1189			60	452	453

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1190			44	454	455
B-1191			47	436	437
B-1192			50	402	403
B-1193			62	462	463
B-1194			49	450	451
B-1195			61	472	473
B-1196			52	428	429

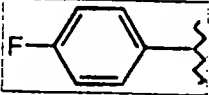
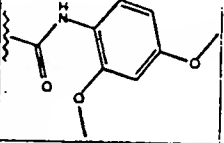
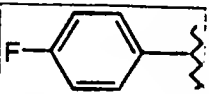
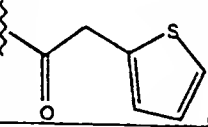
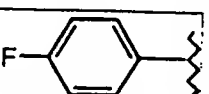
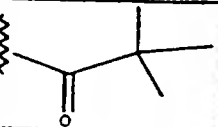
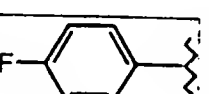
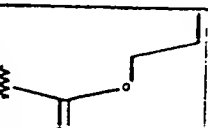
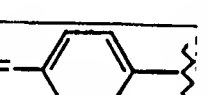
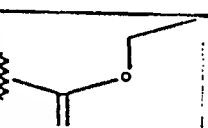
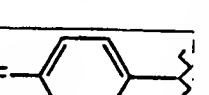
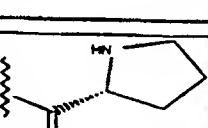
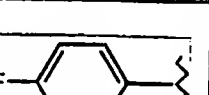
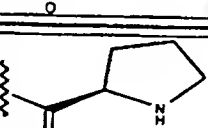
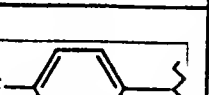
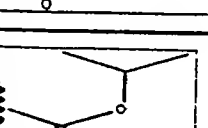
Example#	R <sup>2</sup>	R <sup>J</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1197			54	454	455
B-1198			44	402	403
B-1199			67	416	417
B-1200			45	388	389
B-1201			52	374	375
B-1202			100	466	467
B-1203			91	442	443
B-1204			100	450	451
B-1205			83	496	497
B-1206			97	381	382

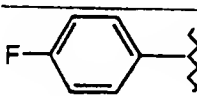
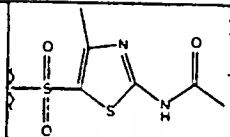
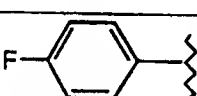
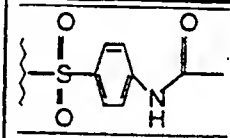
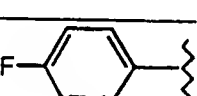
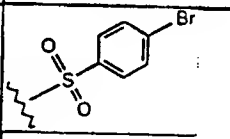
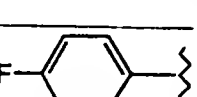
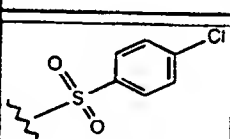
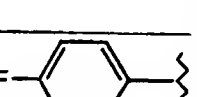
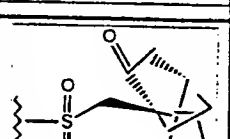
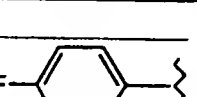
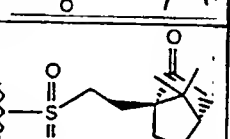
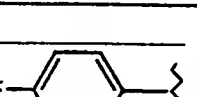
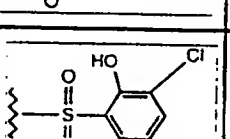
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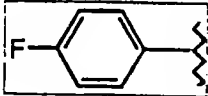
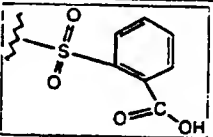
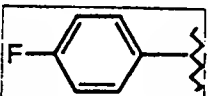
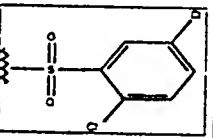
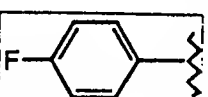
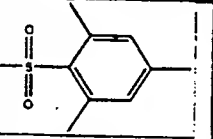
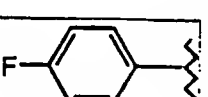
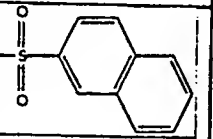
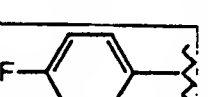
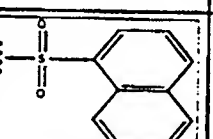
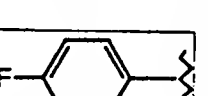
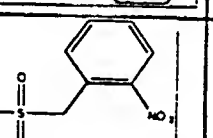
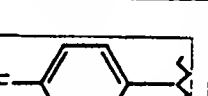
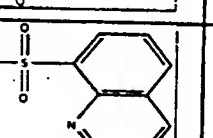
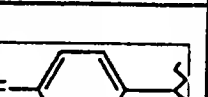
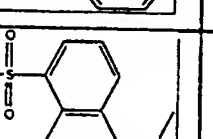

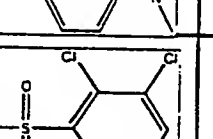

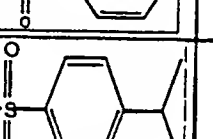
Example#	R <sup>2</sup>	R <sup>J</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1207			100	339	340
B-1208			90	429	430
B-1209			69	393	394
B-1210			35	409	410
B-1211			100	433	434
B-1212			83	367	368
B-1213			78	353	354
B-1214			68	429	430
B-1215			65	433	434
B-1216			91	443	444

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1217			99	379	380
B-1218			92	381	382
B-1219			74	443	444
B-1220			67	415	416
B-1221			14	443	444
B-1222			19	443	444
B-1223			71	433	434
B-1224			100	445	446
B-1225			75	395	396
B-1226			58	367	368

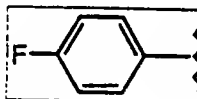
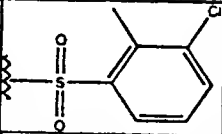
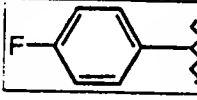
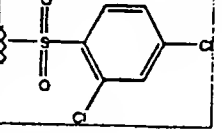
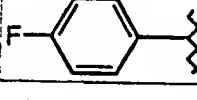
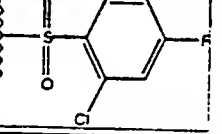
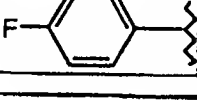
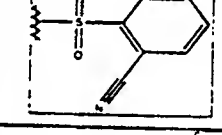
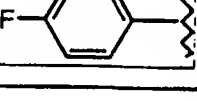
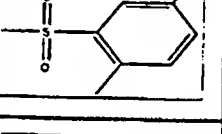
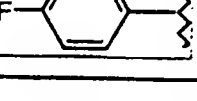
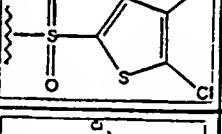
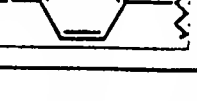
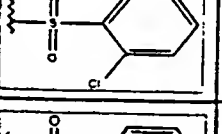
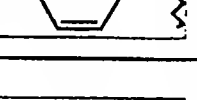
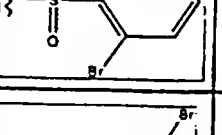
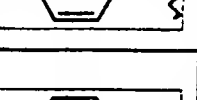
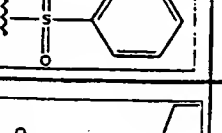
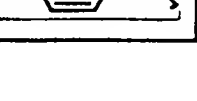
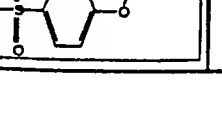
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Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1227			98	475	476
B-1228			71	420	421
B-1229			85	380	381
B-1230			10	382	-
B-1231			66	368	369
B-1232			100	393	394
B-1233			96	393	394
B-1234			66	382	383

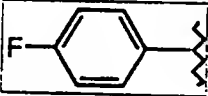
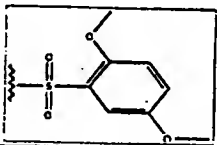
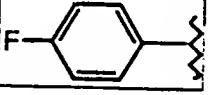
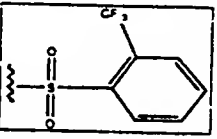
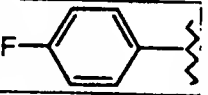
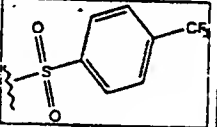
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1235			50	514	515
B-1236			100	493	494
B-1237			91	514	515
B-1238			100	470	471
B-1239			71	510	511
B-1240			27	510	511
B-1241			73	520	

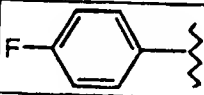
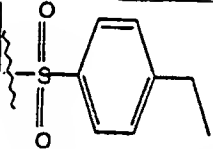
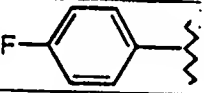
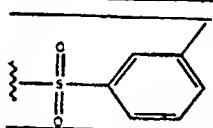
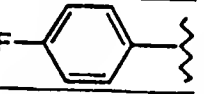
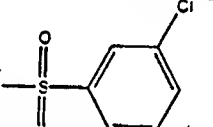
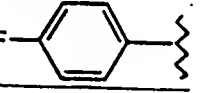
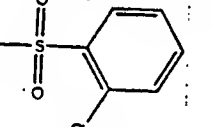
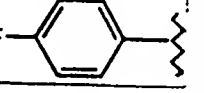
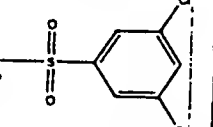
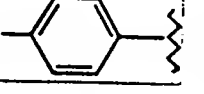
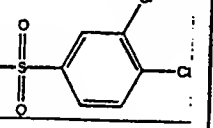
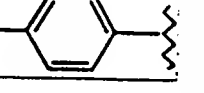
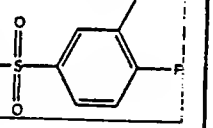
Example#	R <sup>2</sup>	R <sup>J</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1242			26	480	481
B-1243			100	504	
B-1244			52	478	479
B-1245			100	486	487
B-1246			56	486	487
B-1247			43	495	496
B-1248			61	487	488
B-1249			32	529	530
B-1250			56	504	505
B-1251			58	478	479


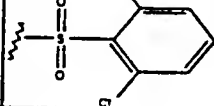
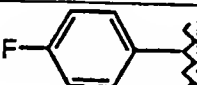
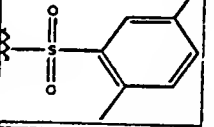
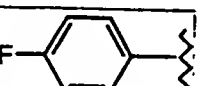
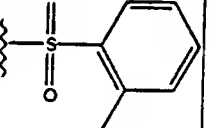
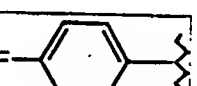
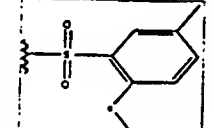
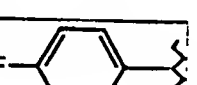
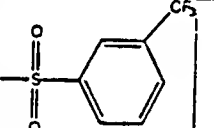
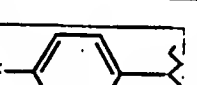
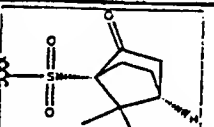
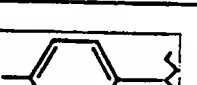
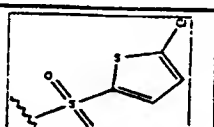

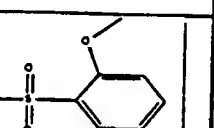
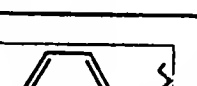
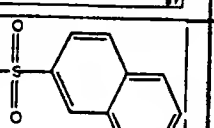

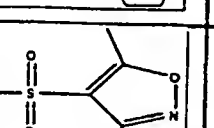
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Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1252			98	484	485
B-1253			59	504	505
B-1254			100	488	489
B-1255			96	461	
B-1256			79	468	469
B-1257			63	510	511
B-1258			100	504	505
B-1259			95	514	515
B-1260			92	514	515
B-1261			98	508	509

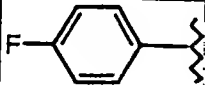
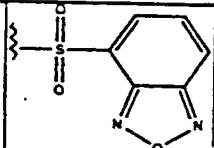
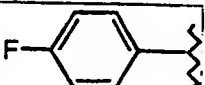
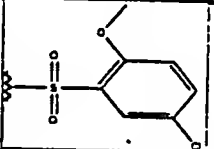
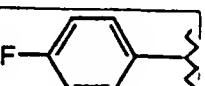
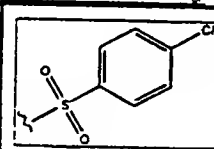
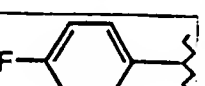
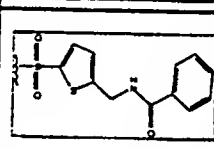
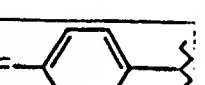
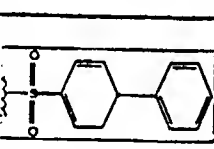
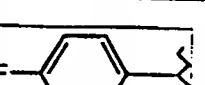
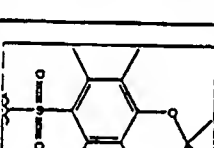

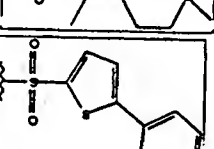

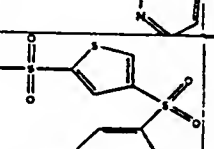

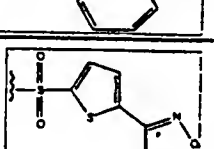

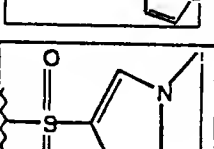
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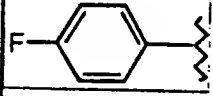
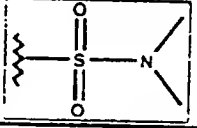
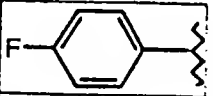
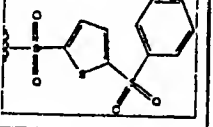
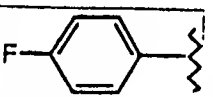
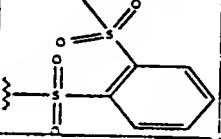
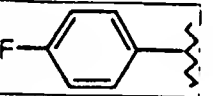
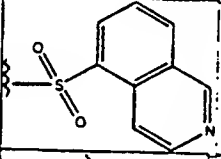
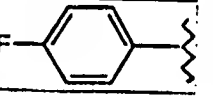
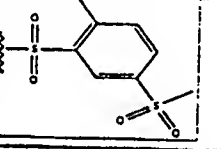
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1262			97	496	497
B-1263			100	504	505
B-1264			100	504	505

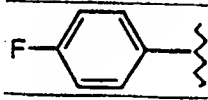
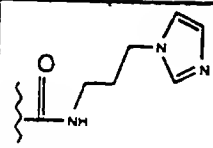
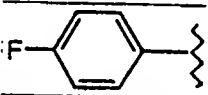
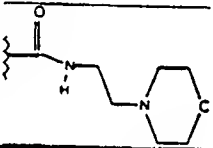
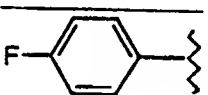
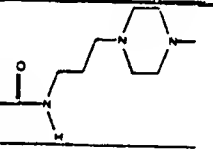
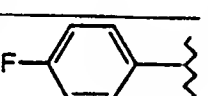
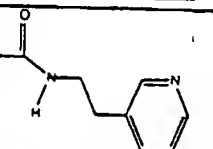
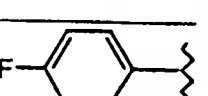
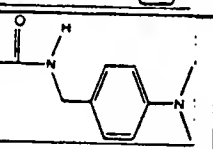
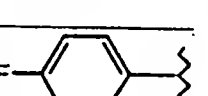
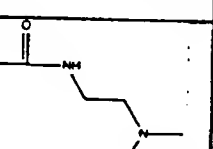
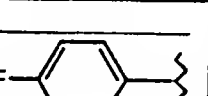
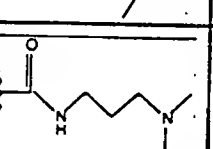
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1265			100	464	465
B-1266			79	466	451
B-1267			100	470	471
B-1268			87	470	471
B-1269			100	504	505
B-1270			100	504	505
B-1271			56	488	489

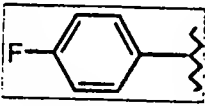
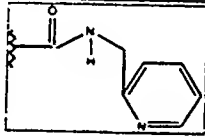
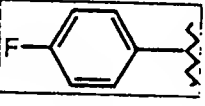
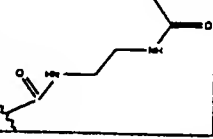
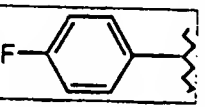
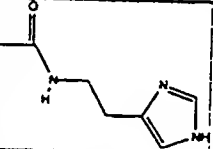
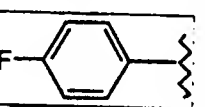
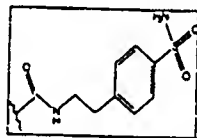
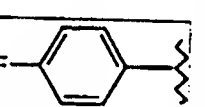
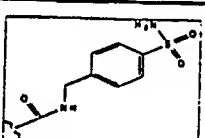
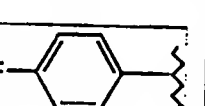
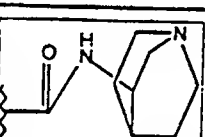
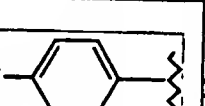
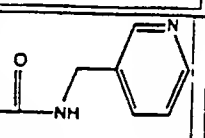
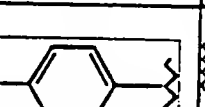
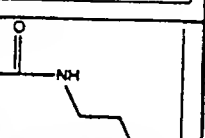
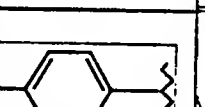
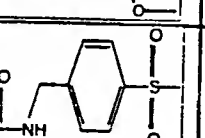
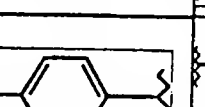

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1272			98	484	485
B-1273			90	464	465
B-1274			87	450	451
B-1275			94	480	481
B-1276			100	504	505
B-1277			60	496	511
B-1278			68	476	477
B-1279			100	544	545
B-1280			68	486	-
B-1281			98	455	456

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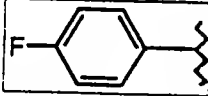
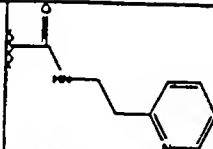
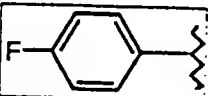
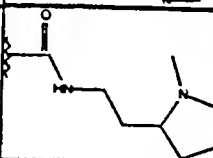
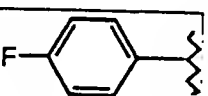
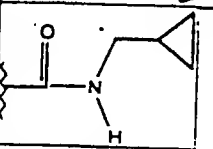
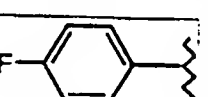
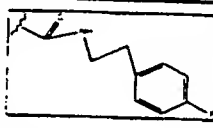
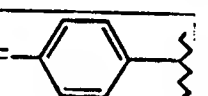
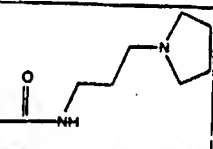
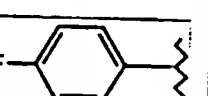
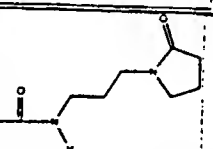
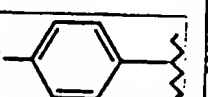
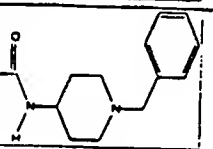
Example#	R <sup>2</sup>	R <sup>J</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1282			100	478	479
B-1283			58	500	501
B-1284			58	461	462
B-1285			65	575	576
B-1286			87	512	513
B-1287			79	562	563
B-1288			100	519	520
B-1289			77	582	583
B-1290			100	509	510
B-1291			91	440	441

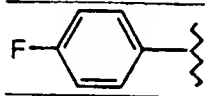
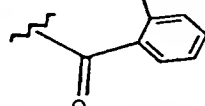
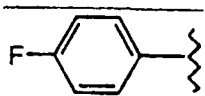
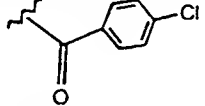
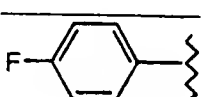
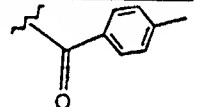
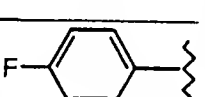
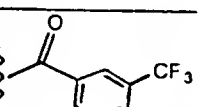
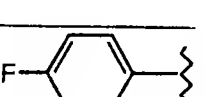
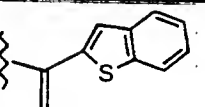
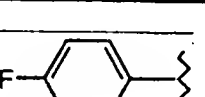
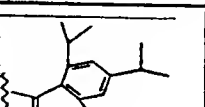
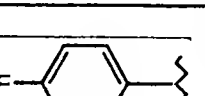
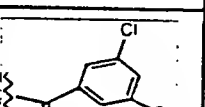
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1292			35	403	404
B-1293			73	582	583
B-1294			49	514	515
B-1295			48	487	-
B-1296			76	528	529

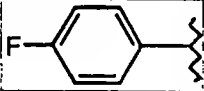
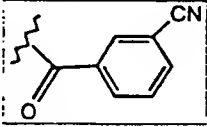
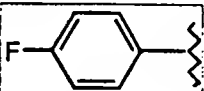
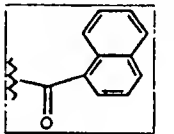
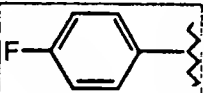
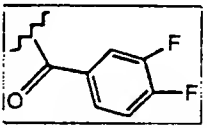
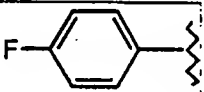
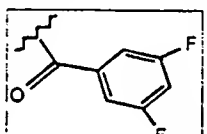
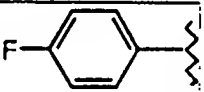
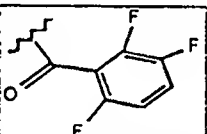
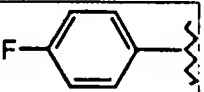
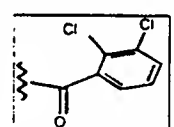
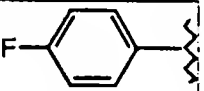
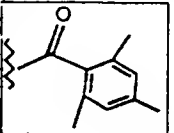
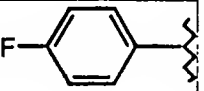
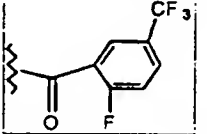
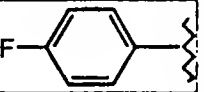
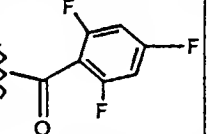
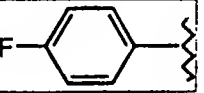
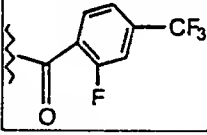
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1297			62	447	448
B-1298			66	452	453
B-1299			65	479	431
B-1300			71	444	445
B-1301			100	472	473
B-1302			75	410	411
B-1303			74	424	425

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1304			11	430	431
B-1305			2	424	-
B-1306			30	433	434
B-1307			100	522	523
B-1308			100	508	509
B-1309			100	448	449
B-1310			26	430	431
B-1311			45	397	398
B-1312			14	507	508
B-1313			67	450	451

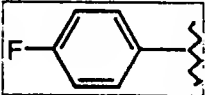
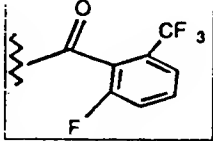
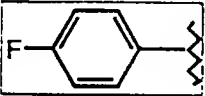
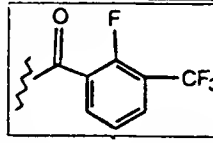
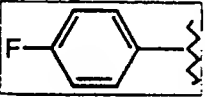
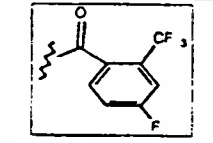
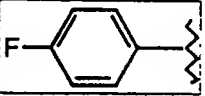
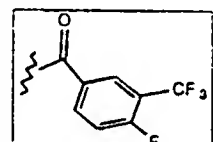
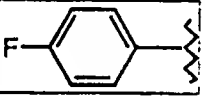
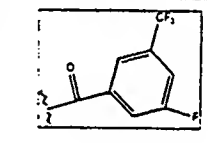
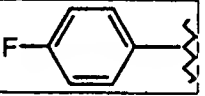
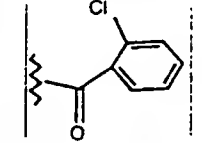
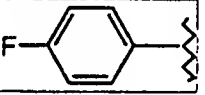
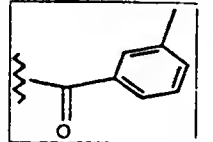
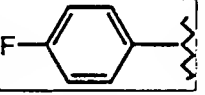
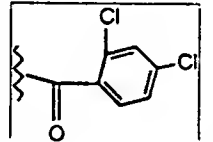
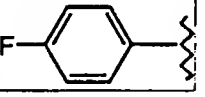
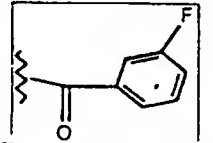
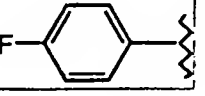
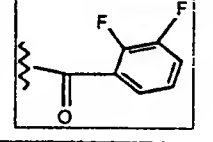
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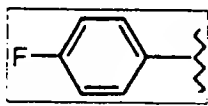
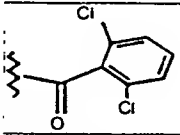
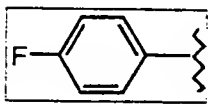
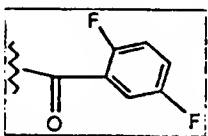
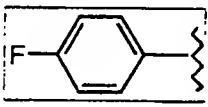
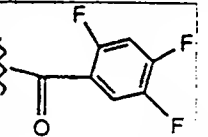
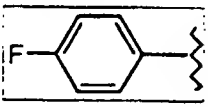
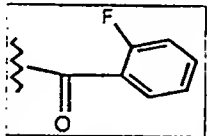
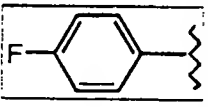
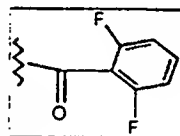
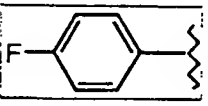
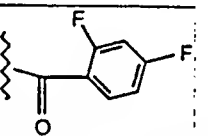
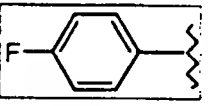
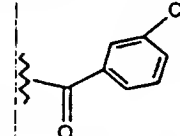
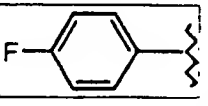
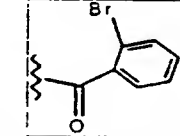
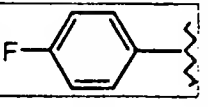
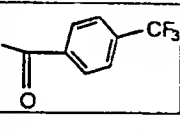
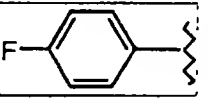
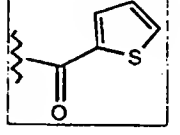
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1314			69	444	445
B-1315			57	450	451
B-1316			75	393	394
B-1317			100	461	462
B-1318			31	450	451
B-1319			23	464	465
B-1320			59	512	513

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1321			63	414	415
B-1322			45	434	435
B-1323			53	414	415
B-1324			32	468	469
B-1325			45	456	457
B-1326			50	526	527
B-1327			55	468	469

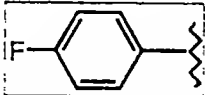
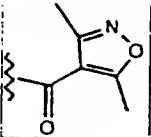
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1328			29	425	426
B-1329			67	450	451
B-1330			59	436	437
B-1331			45	436	437
B-1332			81	454	455
B-1333			23	468	469
B-1334			53	442	443
B-1335			81	486	487
B-1336			69	454	455
B-1337			67	486	487

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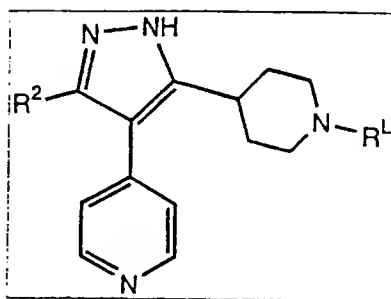
Example#	R <sup>2</sup>	R <sup>J</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1338			39	486	487
B-1339			61	486	487
B-1340			49	486	487
B-1341			55	486	487
B-1342			51	486	487
B-1343			72	434	435
B-1344			52	414	415
B-1345			43	468	469
B-1346			40	418	419
B-1347			67	436	437

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1348			39	468	469
B-1349			68	436	437
B-1350			73	454	455
B-1351			54	418	419
B-1352			77	436	437
B-1353			66	436	437
B-1354			58	434	435
B-1355			77	478	479
B-1356			50	468	469
B-1357			36	406	407

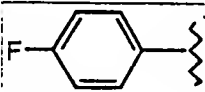
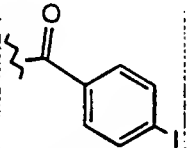
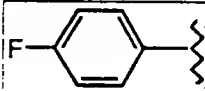
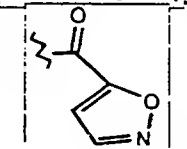
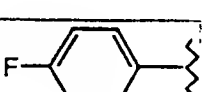
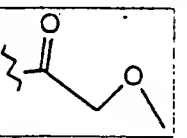
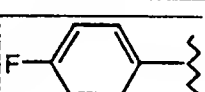
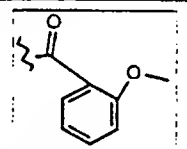
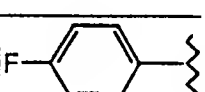
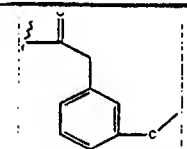
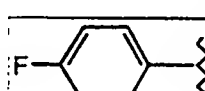
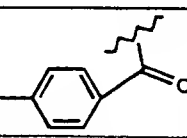
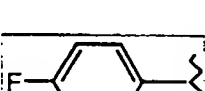
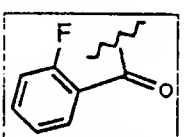
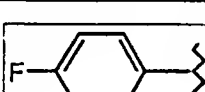
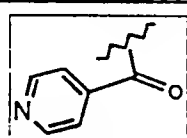
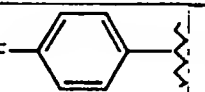
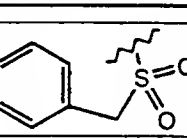
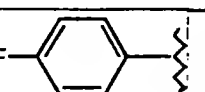
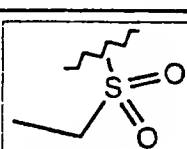
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Example#	R <sup>2</sup>	R <sup>J</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1358			39	419	420

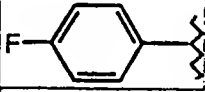
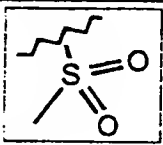
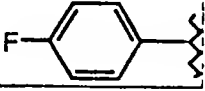
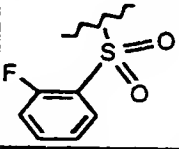
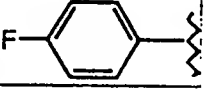
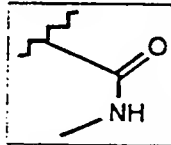
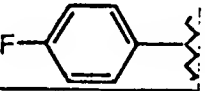
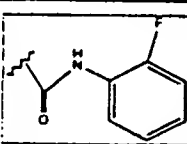
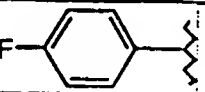
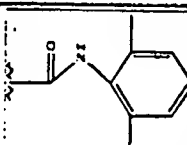
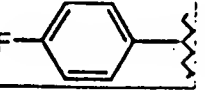
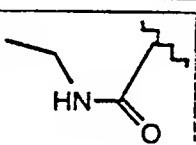
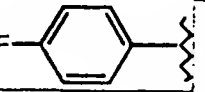
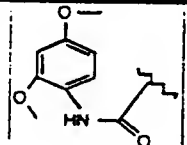
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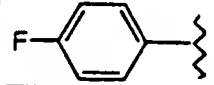
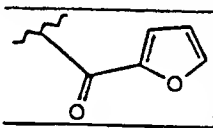
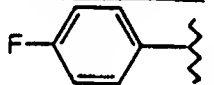
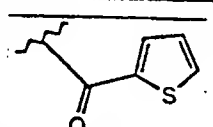
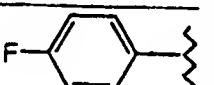
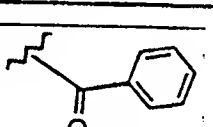
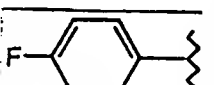
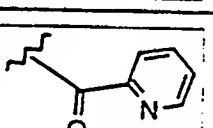
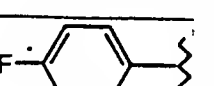
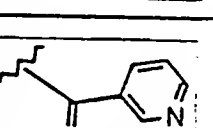
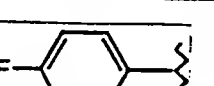
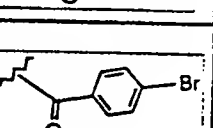
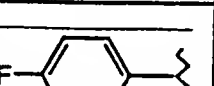
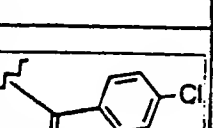


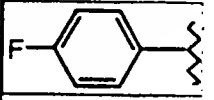
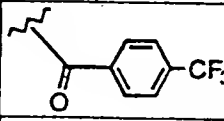
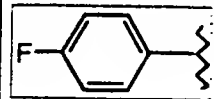
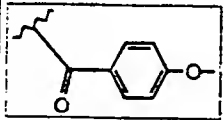
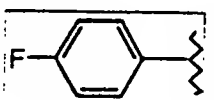
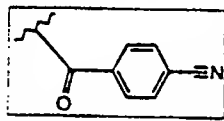
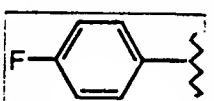
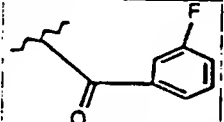
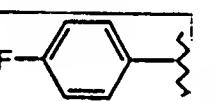
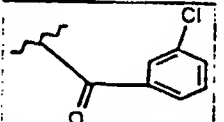
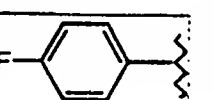
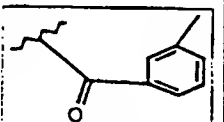
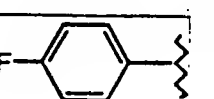
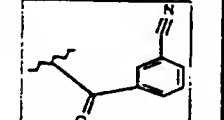
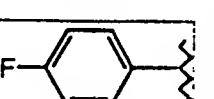
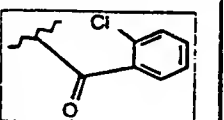
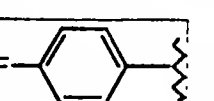
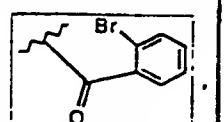
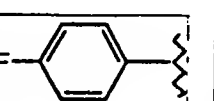
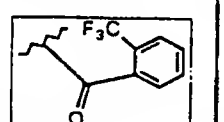
Example#	R <sup>2</sup>	R <sup>L</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1359			95	552	553
B-1360			77	444	445
B-1361			100	392	393
B-1362			85	406	407
B-1363			100	364	365
B-1364			99	390	391
B-1365			92	504	505

Example#	R <sup>2</sup>	R <sup>L</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1366			100	552	553
B-1367			100	417	418
B-1368			86	394	395
B-1369			100	456	457
B-1370			100	470	471
B-1371			77	440	441
B-1372			100	444	445
B-1373			42	427	428
B-1374			60	476	477
B-1375			94	414	415

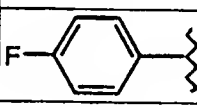
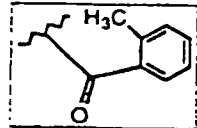
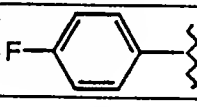
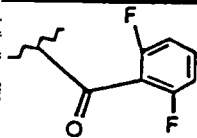
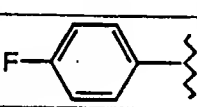
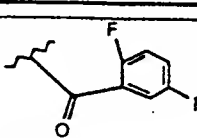
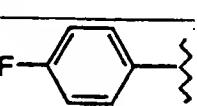
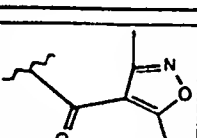
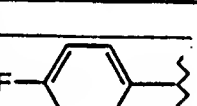
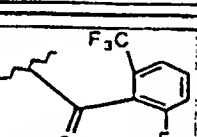
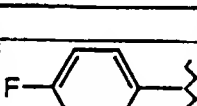
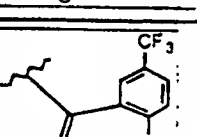
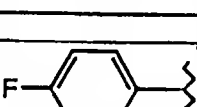
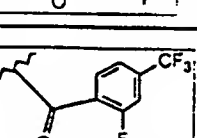
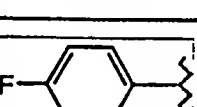
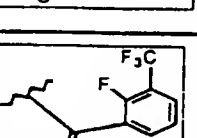
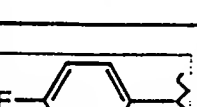
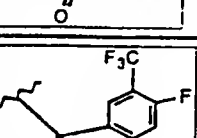

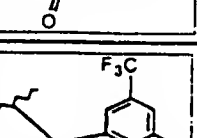
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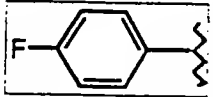
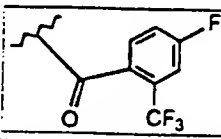
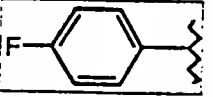
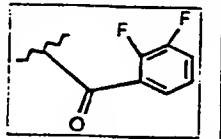
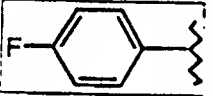
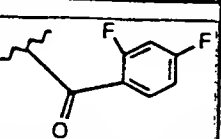
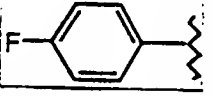
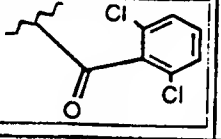
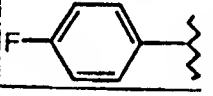
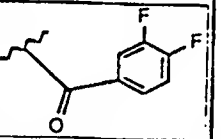
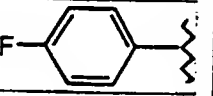
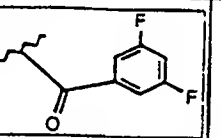
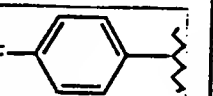
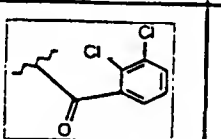
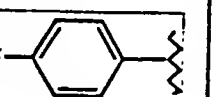
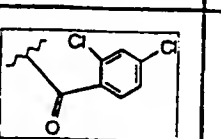
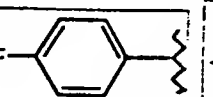
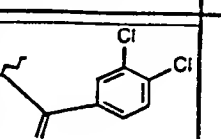
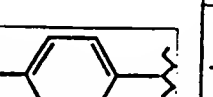
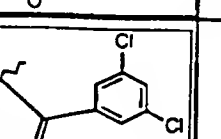
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1376			87	400	401
B-1377			100	480	481
B-1378			95	379	380
B-1379			93	459	460
B-1380			89	469	470
B-1381			84	393	394
B-1382			85	501	502

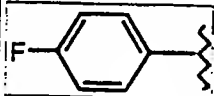
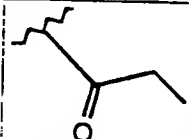
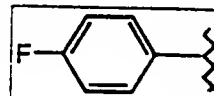
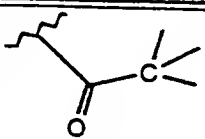
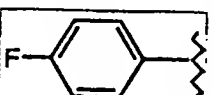
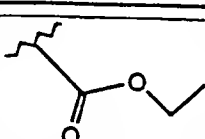
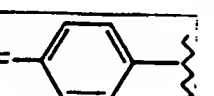
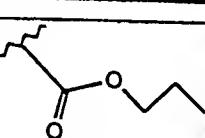
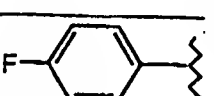
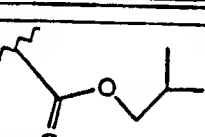
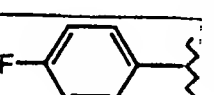
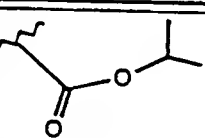
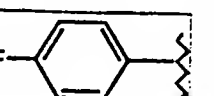
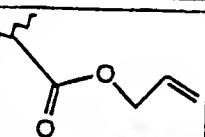
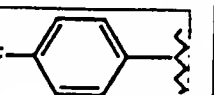
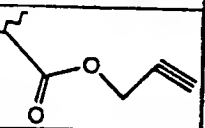
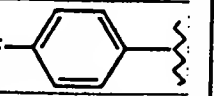
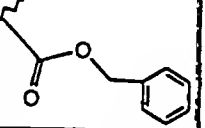
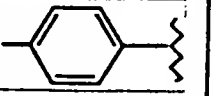
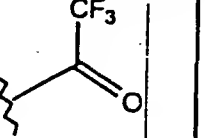
Example#	R <sup>2</sup>	R <sup>L</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1383			46	416	417
B-1384			56	432	433
B-1385			59	426	427
B-1386			50	427	428
B-1387			12	427	428
B-1388			66	504	505
B-1389			48	460	461

Example#	R <sup>2</sup>	R <sup>L</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1390			44	494	495
B-1391			50	456	457
B-1392			47	451	452
B-1393			44	444	445
B-1394			52	460	461
B-1395			77	440	441
B-1396			58	451	452
B-1397			64	460	461
B-1398			65	504	505
B-1399			50	494	495

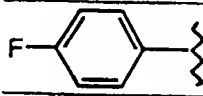
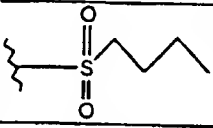
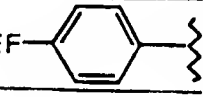
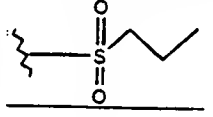
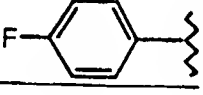
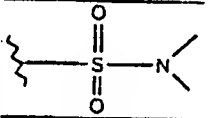
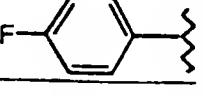
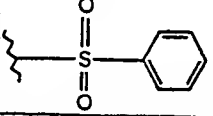
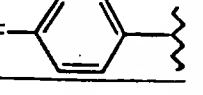
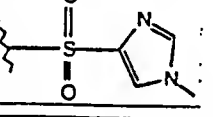
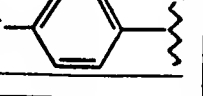
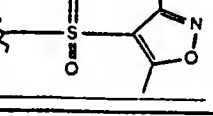
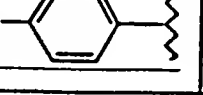
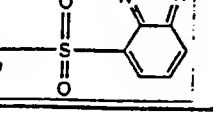
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Example#	R <sup>2</sup>	R <sup>L</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1400			74	440	441
B-1401			76	462	463
B-1402			65	462	463
B-1403			64	445	446
B-1404			70	512	513
B-1405			57	512	513
B-1406			73	512	513
B-1407			80	512	513
B-1408			2	512	513
B-1409			62	512	513

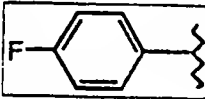
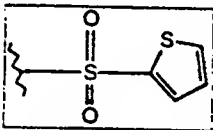
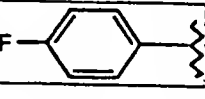
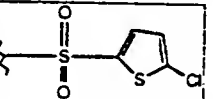
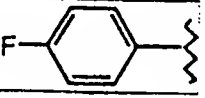
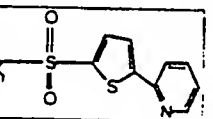
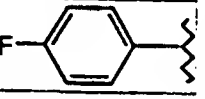
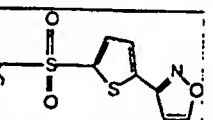
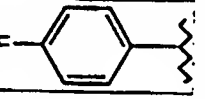
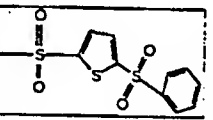
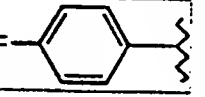
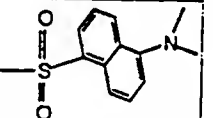
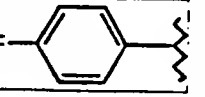
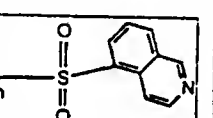
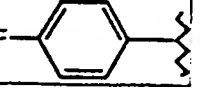
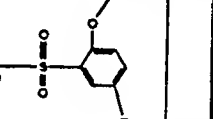
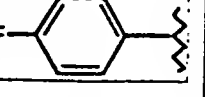
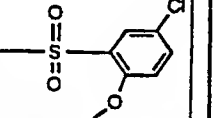
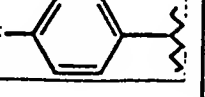
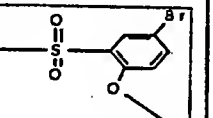
Example#	R <sup>2</sup>	R <sup>L</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1410			42	512	513
B-1411			19	462	463
B-1412			74	462	463
B-1413			75	494	495
B-1414			68	462	463
B-1415			48	462	463
B-1416			48	494	495
B-1417			57	494	495
B-1418			49	494	495
B-1419			39	494	495

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1420			72	378	379
B-1421			74	406	407
B-1422			68	394	395
B-1423			57	408	409
B-1424			77	422	423
B-1425			26	408	409
B-1426			41	406	407
B-1427			37	404	405
B-1428			60	456	457
B-1429			2	418	419

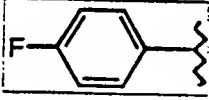
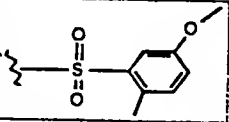
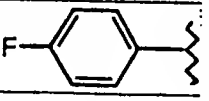
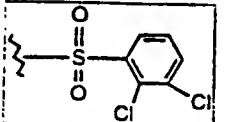
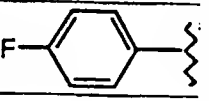
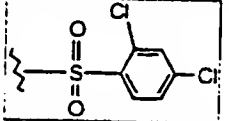
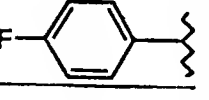
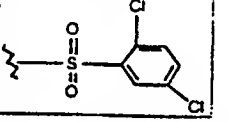
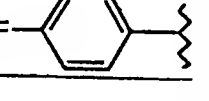
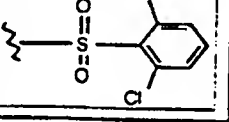
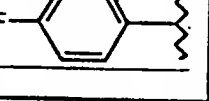
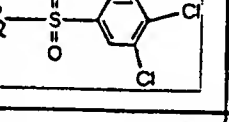
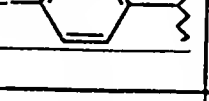
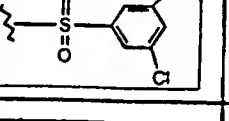
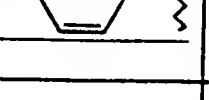
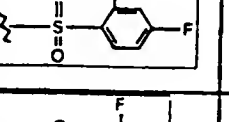

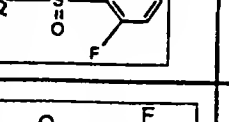
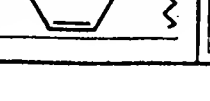
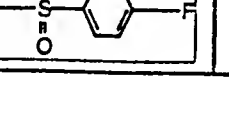
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Example#	R <sup>2</sup>	R <sup>L</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1430			61	442	443
B-1431			64	428	429
B-1432			71	429	430
B-1433			74	462	463
B-1434			88	466	467
B-1435			75	481	482
B-1436			71	504	505

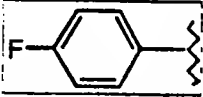
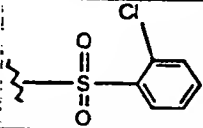
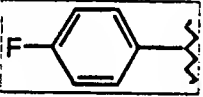
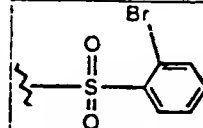
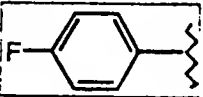
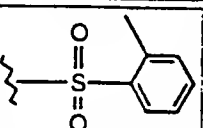
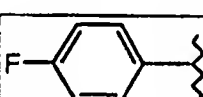
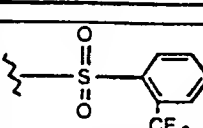
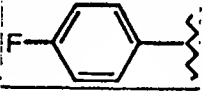
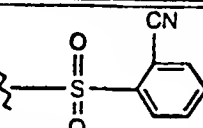
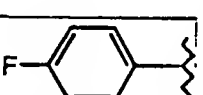
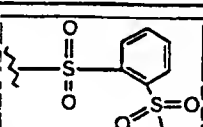
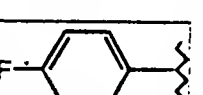
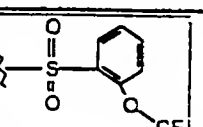
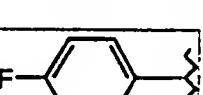
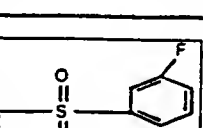
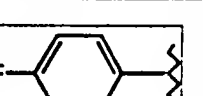
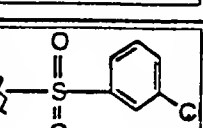
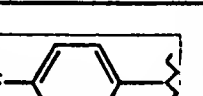
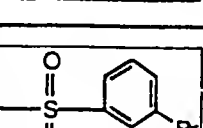
757

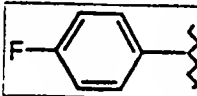
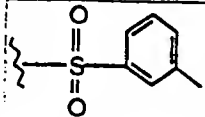
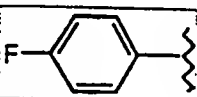
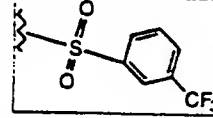
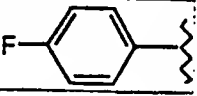
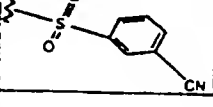
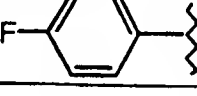
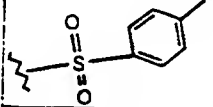
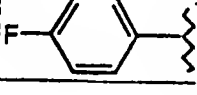
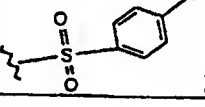
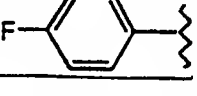
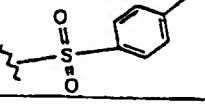
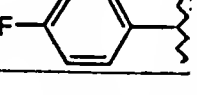
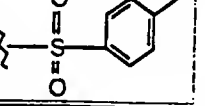
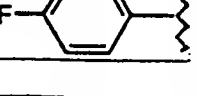
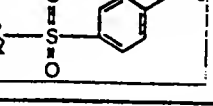
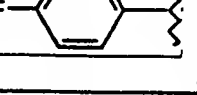
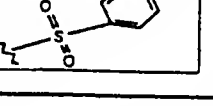

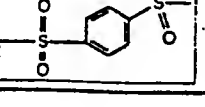
Example#	R <sup>2</sup>	R <sup>L</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1437			63	468	469
B-1438			78	502	503
B-1439			70	545	546
B-1440			62	535	536
B-1441			82	608	
B-1442			79	555	556
B-1443			28	513	514
B-1444			75	522	523
B-1445			74	526	527
B-1446			70	570	571

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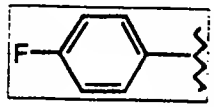
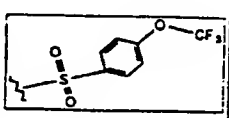
Example#	R <sup>2</sup>	R <sup>L</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1447			73	506	507
B-1448			76	530	531
B-1449			82	530	531
B-1450			83	530	531
B-1451			74	530	531
B-1452			76	530	531
B-1453			73	530	531
B-1454			81	498	499
B-1455			83	498	499
B-1456			78	498	499

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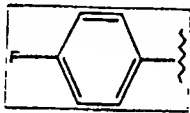
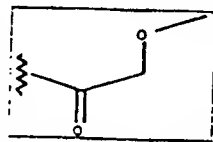
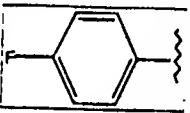
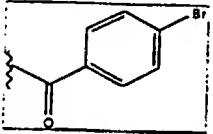

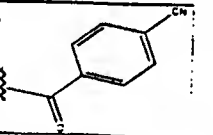
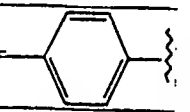
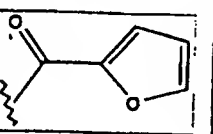
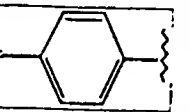
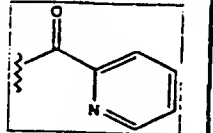

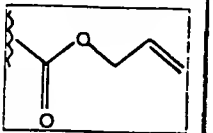
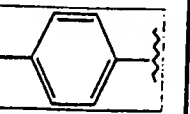
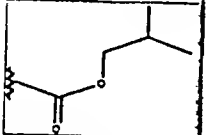
Example#	R <sup>2</sup>	R <sup>L</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1457			74	496	497
B-1458			82	540	541
B-1459			80	476	477
B-1460			78	530	531
B-1461			82	487	488
B-1462			71	540	541
B-1463			78	546	547
B-1464			83	480	481
B-1465			84	496	497
B-1466			80	540	541

Example#	R <sup>2</sup>	R <sup>L</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1467			79	476	477
B-1468			79	530	531
B-1469			75	487	488
B-1470			80	480	481
B-1471			74	496	497
B-1472			75	540	541
B-1473			77	476	477
B-1474			81	530	531
B-1475			70	487	488
B-1476			54	540	541


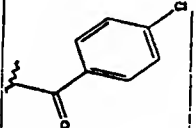

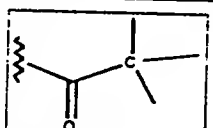
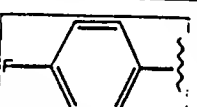
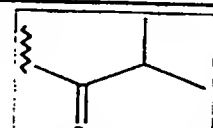
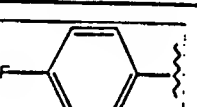
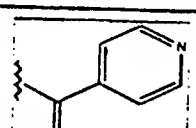
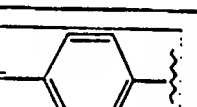
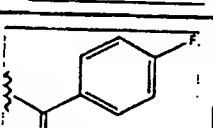
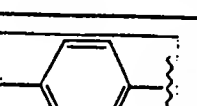
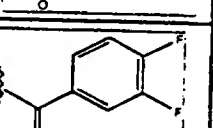
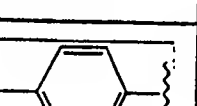
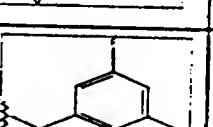
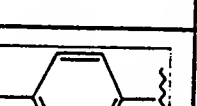
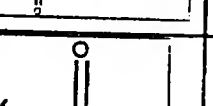

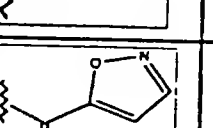


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Example#	R <sup>2</sup>	R <sup>L</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1477			79	546	547

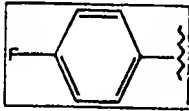
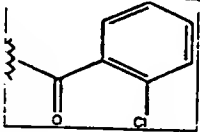
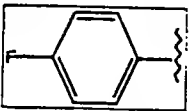
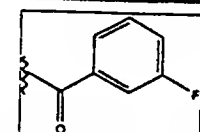

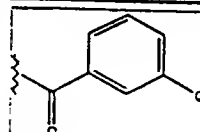
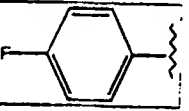
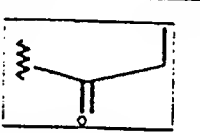

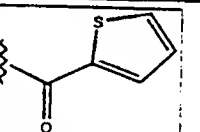
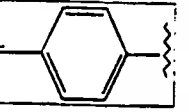
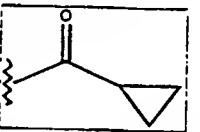
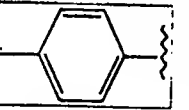
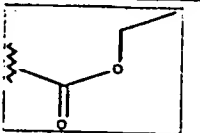
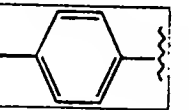
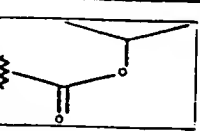

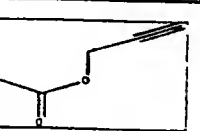
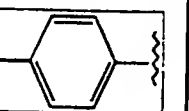
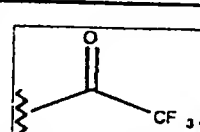
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Example#	R <sup>2</sup>	R <sup>L</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1478			87	394	395
B-1479			41	504	505
B-1480			87	451	452
B-1481			18	416	417
B-1482			77	427	428
B-1483			74	406	407
B-1484			82	422	423


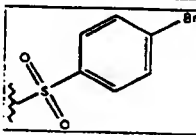
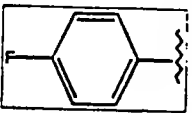
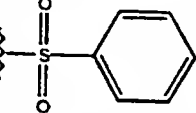
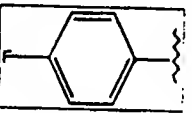
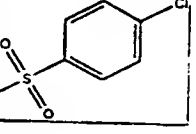
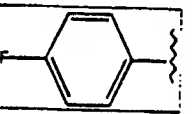
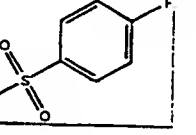
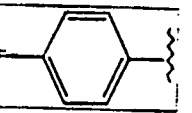
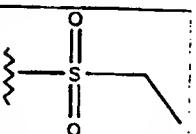
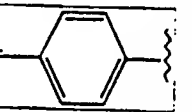
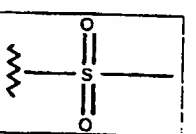

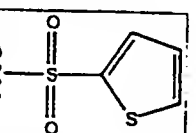

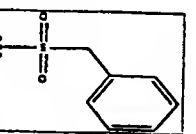

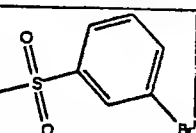
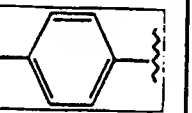
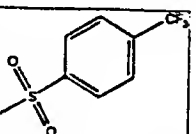
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Example#	R <sup>2</sup>	R <sup>L</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1485			85	460	461
B-1486			64	406	407
B-1487			71	392	393
B-1488			82	427	428
B-1489			87	444	445
B-1490			81	462	463
B-1491			87	462	463
B-1492			69	364	365
B-1493			53	417	418
B-1494			17	426	427


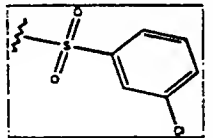
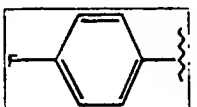
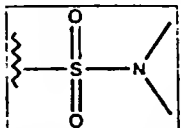
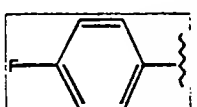
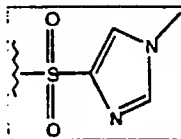
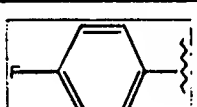
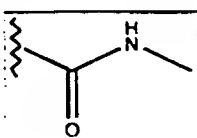
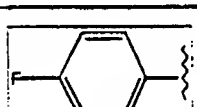
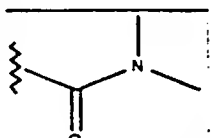
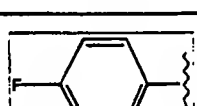
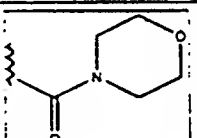
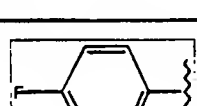
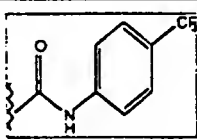
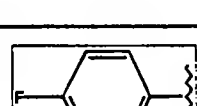
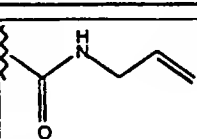

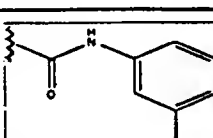

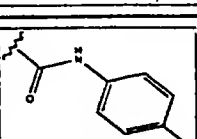
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Example#	R <sup>2</sup>	R <sup>L</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1495			79	460	461
B-1496			80	444	445
B-1497			82	460	461
B-1498			72	378	379
B-1499			70	432	433
B-1500			68	390	391
B-1501			63	394	395
B-1502			78	408	409
B-1503			55	404	405
B-1504			39	418	419

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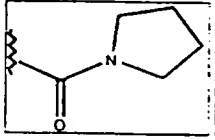
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1505			69	540	541
B-1506			69	462	463
B-1507			70	496	497
B-1508			65	480	481
B-1509			56	414	415
B-1510			62	400	401
B-1511			30	468	469
B-1512			50	476	477
B-1513			44	540	541
B-1514			42	530	531

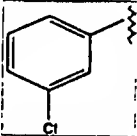
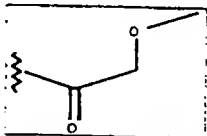
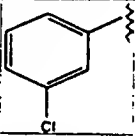
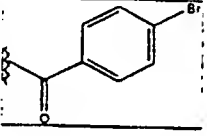
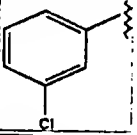
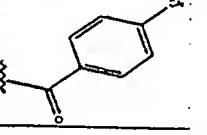
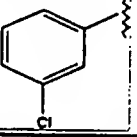
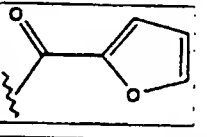
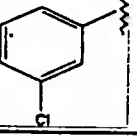
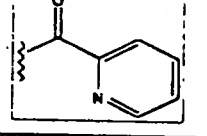
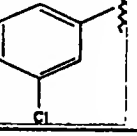
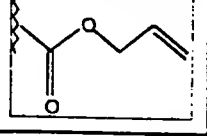
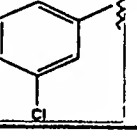
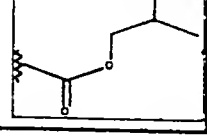
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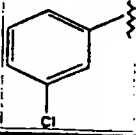
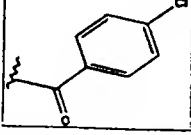
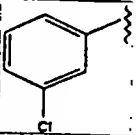
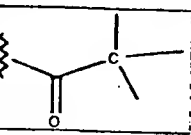
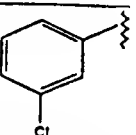
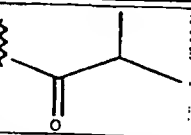
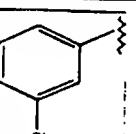
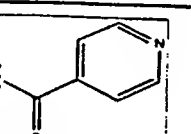
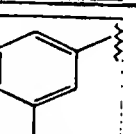
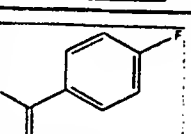
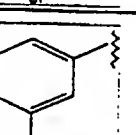
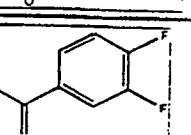
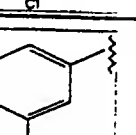
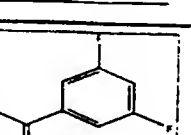
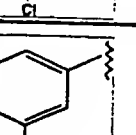
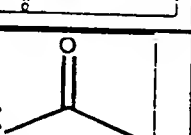
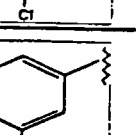
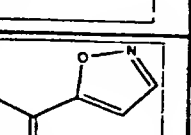
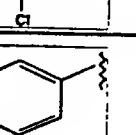
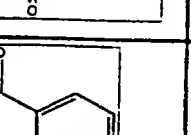
Example#	R <sup>2</sup>	R <sup>L</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1515			68	496	497
B-1516			27	429	430
B-1517			92	466	467
B-1518			33	379	380
B-1519			50	393	394
B-1520			82	435	436
B-1521			86	509	510
B-1522			12	405	406
B-1523			59	459	460
B-1524			81	459	460

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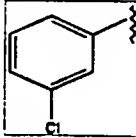
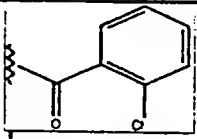
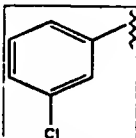
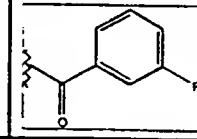
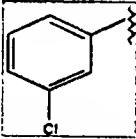
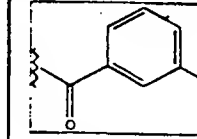
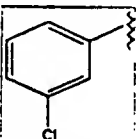
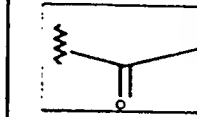
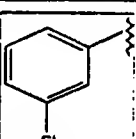
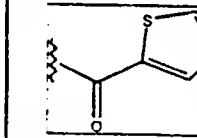
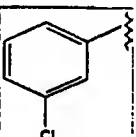
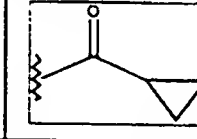
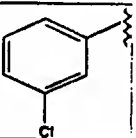
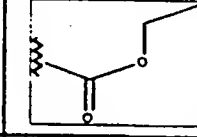
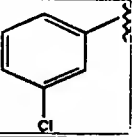
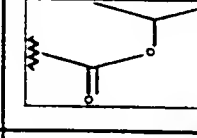
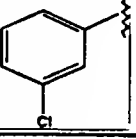
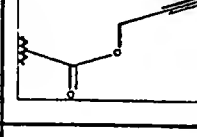
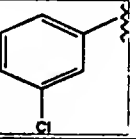
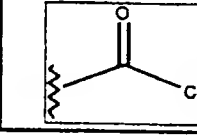
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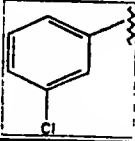
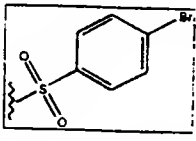
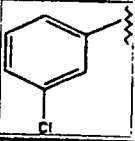
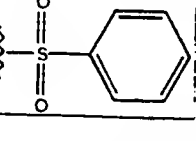
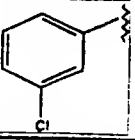
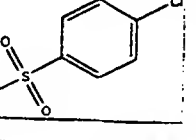
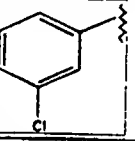
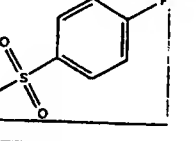
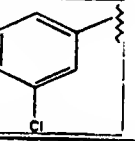
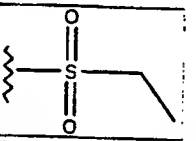
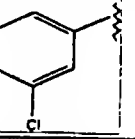
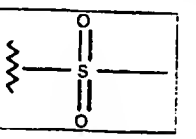
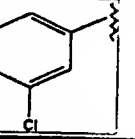
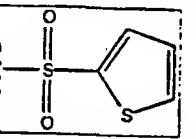
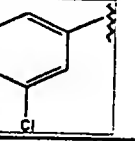
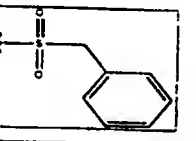
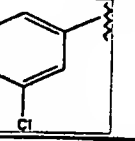
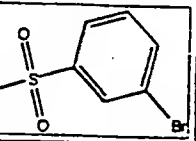
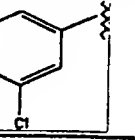
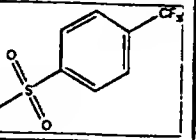
Example#	R <sup>2</sup>	R <sup>L</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1525			57	419	420

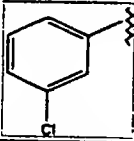
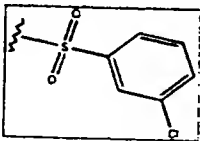
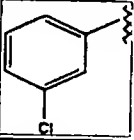
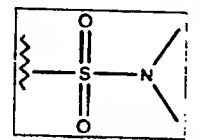
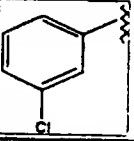
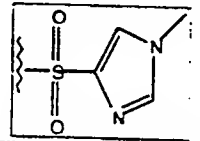
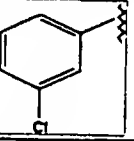
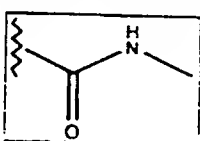
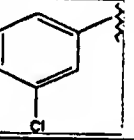
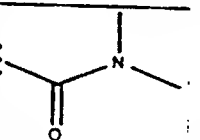
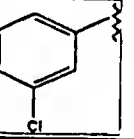
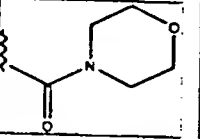
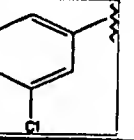
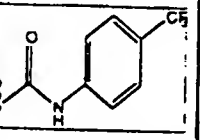
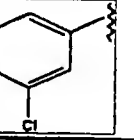
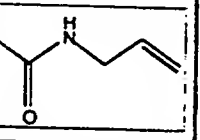
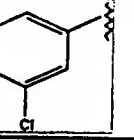
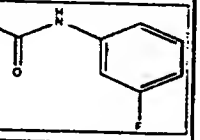
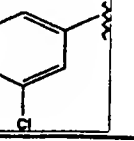
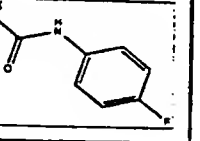
Example#	R <sup>2</sup>	R <sup>L</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1526			73	410	411
B-1527			66	520	521
B-1528			91	467	468
B-1529			73	432	433
B-1530			91	443	444
B-1531			74	422	423
B-1532			68	438	439

Example#	R <sup>2</sup>	R <sup>L</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1533			84	476	477
B-1534			72	422	423
B-1535			78	408	409
B-1536			77	443	444
B-1537			86	460	461
B-1538			74	478	479
B-1539			85	478	479
B-1540			71	380	381
B-1541			71	433	434
B-1542			89	442	443

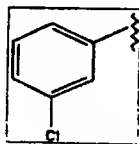
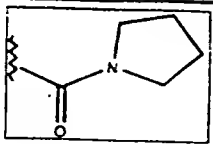
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Example#	R <sup>2</sup>	R <sup>L</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1543			82	476	477
B-1544			76	460	461
B-1545			77	476	477
B-1546			76	394	395
B-1547			58	448	449
B-1548			83	406	407
B-1549			67	410	411
B-1550			37	424	425
B-1551			55	420	421
B-1552			23	434	435

Example#	R <sup>2</sup>	R <sup>L</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1553			83	556	557
B-1554			84	478	479
B-1555			93	512	513
B-1556			83	496	497
B-1557			62	430	431
B-1558			45	416	417
B-1559			67	484	485
B-1560			16	492	493
B-1561			84	556	557
B-1562			74	546	547

Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1563			72	512	513
B-1564			57	445	446
B-1565			64	482	483
B-1566			71	395	396
B-1567			54	409	410
B-1568			76	451	452
B-1569			70	525	526
B-1570			79	421	422
B-1571			60	475	476
B-1572			77	475	476

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Example#	R <sup>2</sup>	R <sup>L</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1573			65	435	436

775

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Proton NMR data for selected members from Examples B-0001 through B-1573 are shown in the following table.

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Plate ID	<sup>1</sup> H NMR(solvent), d ppm
B-0120	(DMF-d7) d 8.53(bd, J = 4.99Hz, 2H), 7.44-7.24(m, 11H), 4.41(s, 2H), 4.31(br, 2H)
B-0224	(DMF-d7) d 8.56(bd, J = 4.98Hz, 2H), 7.78-7.69(m, 4H), 7.39-7.19(m, 6H), 4.23(br, 2H)
B-0235	(DMF-d7) d 8.47(br, 2H), 7.91-7.75(m, 3H), 7.57-7.53(m, 1H), 7.38-7.34(m, 2H), 7.21-7.13(m, 4H), 4.20(br, 2H)
B-0244	(CDCl <sub>3</sub> /CD <sub>3</sub> OD) d 8.38(d, J = 5.38 Hz, 1H), 7.62-7.32(m, 9H), 7.04-6.95(m, 4H), 6.86-6.80(m, 2H), 4.52(q, J = 6.96 Hz, 1H), 1.40(d, J = 6.88 Hz, 3H)
B-0256	(DMF-d7) d 8.45(bd, J = 2.85, 2H), 7.87(br s, 4H), 7.76-7.75(m, 2H), 7.53-7.33(m, 5H), 7.18-7.13(br, 4H)
B-0426	(DMF-d7), 1.32(br, 3H), 1.67(br, 3H), 4.17(br, 2H), 5.12(br, 1H), 7.50(m, 6H), 8.77(m, 2H), 13.54(br, 1H).
B-0438	(DMSO), 1.14(t, J = 6.9 Hz, 3H), 4.54(m, 1H), 6.99(br, 2H), 7.21(br, 4H), 7.45(s, 1H), 7.61(q, J = 8.7 Hz, 2H), 8.52(d, J = 5.2 Hz, 2H).
B-0466	(DMF-d7), 1.61(brd, J = 30.6 Hz, 3H), 4.61 (br, 1H), 7.25(m, 6H), 7.65(m, 3H), 8.59(br, 2H), 13.34(brd, J = 34.8 Hz, 1H).
B-0473	(CD <sub>3</sub> OD), 1.53(d, J = 7.2 Hz, 3H), 4.59(q, J = 7.2 Hz, 1H), 6.88(d, J = 4 Hz, 1H), 7.09(m, 3H), 7.15(dd, J = 4.4, 1.6 Hz, 2H), 7.26(m, 2H), 8.46(d, J = 6.0 Hz, 2H).
B-0477	(DMF), 1.80(br, 3H), 2.35(s, 1H), 4.98(br, 1H), 7.38(m, 6H), 7.85(m, 2H), 8.45(br, 1H), 8.75(d, J = 6.0 Hz, 2H).
B-0479	(Methanol-d <sub>4</sub> ), 1.57(d, J = 5.6 Hz, 3H), 4.74(br, 1H), 7.23(m, 4H), 7.60(m, 2H), 7.81(m, 4H), 8.67(br, 2H).
B-0487	(DMF), 1.78(s, 3H), 2.76(br, 6H), 4.85(br, 1H), 7.42(br, 2H), 7.54(br, 2H), 7.66(br, 3H), 8.82(s, 2H).
B-0566	(CD <sub>3</sub> OD), 1.38(d, J = 7.2 Hz, 3H), 4.15(br, 2H), 4.50(br, 1H), 7.04(br, 2H), 7.18(br, 2H), 7.30(m, 7H), 8.45(m, 2H).
B-0569	(CD <sub>3</sub> OD), 1.56(br, 3H), 4.66(q, J = 6.7 Hz, 1H), 7.17(m, 8H), 7.56(m, 2H), 8.47(s, 2H).
B-0574	(Methanol-d <sub>4</sub> ), 1.49(br, 3H), 3.86(br, 3H), 4.60(br, 1H), 6.92(br, 2H), 7.19(br, 2H), 7.31(br, 2H), 7.76(m, 4H), 8.60(br, 2H).
B-0639	(DMF-d7), 1.58(brd, J = 30.0 Hz, 3H), 4.62(br, 1H), 7.25(m, 6H), 7.60(m, 4H), 8.59(br, 2H), 13.30(brd, J = 12.3 Hz).
B-0643	7.18(m, 2H), 7.32(dd, J = 6.0, 4.4 Hz, 1H), 7.70(dd, J = 9.0, 5.8Hz, 1H), 8.43(dd, J = 4.8, 3.2 Hz, 2H).
B-0650	(CD <sub>3</sub> OD), 1.58(br, 3H), 4.62(q, J = 6.6 Hz, 1H), 6.93(br, 1H), 7.17(m, 5H), 7.31(br, 2H), 8.51(br, 2H).
B-0656	(CDCl <sub>3</sub> /CD <sub>3</sub> OD) d 8.48 (d, J = 5.30 Hz, 2H), 7.72-7.59(m, 4H), 7.14-7.10(m, 2H), 7.03-6.97(m, 4H), 4.60(q, J = 7.57Hz, 1H), 1.43(d, J = 7.26Hz, 3H)
B-0663	(CD <sub>3</sub> OD), 1.52(d, J = 6.8 Hz, 3H), 3.75(s, 3H), 7.21(m, 2H), 7.42(m, 2H), 7.57(s, 1H), 7.76(s, 1H), 7.98(br, 2H), 8.76(br, 2H).
B-1165	Hz, 2H), 3.06(m, 1H), 3.43(q, J = 6.1 Hz, 2H), 7.02(m, 2H), 7.14(m, 2H), 7.41(m, 2H), 8.59(d, J = 5.6 Hz, 2H).
B-1169	= 1.6 Hz, 1H), 7.04(t, J = 8.6 Hz, 2H), 7.14(m, 2H), 7.36(m, 2H), 8.39(d, J = 1.8 Hz, 1H), 8.60(m, 2H).
B-1171	6.83(br, 1H), 7.02(t, J = 8.7 Hz, 2H), 7.15(d, J = 5.6 Hz, 2H), 7.40(m, 2H), 8.59(d, J = 5.0 Hz, 2H).

Plate ID	<sup>1</sup> H NMR(solvent), d ppm
B-1179	(CDCl <sub>3</sub> ), 1.94(br, 2H), 2.53(s, 3H), 2.85(t, J = 6.2 Hz, 2H), 3.65(br, 2H), 6.15(br, 1H), 7.04(m, 3H), 7.22(m, 3H), 7.41(br, 4H), 8.60(br, 2H).
B-1183	(CDCl <sub>3</sub> ), 2.00(br, 2H), 2.85(br, 2H), 3.64(br, 2H), 7.03(br, 3H), 7.17(br, 2H), 7.36(br, 2H), 7.66(br, 2H), 8.60(br, 2H), 8.77(br, 2H).
B-1194	(DMSO), 1.76(br, 2H), 2.66(br, 2H), 2.91(br, 2H), 4.30(s, 2H), 7.18(br, 5H), 7.35(m, 6H), 8.54(d, J = 5.8 Hz, 2H).
B-1200	(DMSO), 1.17(br, 3H), 1.76(br, 2H), 2.71(br, 2H), 2.97(br, 4H), 7.18(br, 4H), 7.36(br, 2H), 8.54(br, 2H).
B-1206	(DMSO), 1.03(s, 6H), 1.68(br, 2H), 2.63(br, 2H), 3.00(br, 2H), 3.65(br, 1H), 5.69(m, 2H), 7.16(br, 4H), 7.35(br, 2H), 8.54(br, 2H).
B-1216	(DMSO), 1.75(m, 2H), 2.14(s, 6H), 2.66(br, 2H), 3.10(br, 2H), 7.04(br, 3H), 7.18(br, 4H), 7.35(m, 2H), 7.47(br, 1H), 8.54(d, J = 4.8 Hz, 2H).
B-1226	(DMF), 1.25(br, 3H), 2.01(br, 2H), 3.35(br, 4H), 6.20(s, 1H), 6.30(s, 1H), 7.42(br, 4H), 7.65(br, 2H), 8.77(s, 2H).
B-1360	(DMSO-d <sub>6</sub> ), 1.80(br, 4H), 2.82(br, 1H), 2.94(br, 1H), 3.10(br, 1H), 3.60(br, 1H), 4.54(br, 1H), 7.18(m, 4H), 7.30(m, 4H), 7.46(m, 2H), 8.54(br, 2H).
B-1361	(DMSO-d <sub>6</sub> ), 0.99(br, 6H), 1.73(br, 4H), 2.89(br, 2H), 3.03(m, 1H), 4.04(br, 2H), 4.44(m, 1H), 7.18(m, 4H), 7.30(m, 2H), 8.57(d, J = 4.64 Hz, 2H).
B-1363	(DMSO-d <sub>6</sub> ), 1.78(br, 4H), 2.01(s, 3H), 2.89(br, 1H), 3.05(br, 1H), 3.34(br, 1H), 3.85(br, 1H), 4.48(br, 1H), 7.12(br, 2H), 7.21(br, 2H), 7.30(br, 2H), 8.69(br, 2H).
B-1364	(CDCl <sub>3</sub> ), 0.78(dd, J = 3.0, 2.9 Hz, 2H), 1.00(s, 2H), 1.78(m, 1H), 1.86(b, 4H), 2.64(m, 1H), 2.99(m, 1H), 3.16(m, 1H), 4.33(br, 1H), 4.70(br, 1H), 6.99(m, 2H), 7.14(s, 2H), 7.29(m, 2H), 8.64(s, 2H).
B-1368	(CDCl <sub>3</sub> ), 1.89(s, 4H), 2.65(m, 1H), 2.96(m, 1H), 3.06(m, 1H), 3.43(s, 3H), 3.93(d, J = 13.2 Hz, 1H), 4.09(d, J = 13.5 Hz, 1H), 4.18(d, J = 13.5 Hz, 1H), 4.68(d, J = 12.4 Hz, 1H), 7.60(m, 2H), 7.12(s, 2H), 7.26(m, 2H), 8.63(s, 2H).

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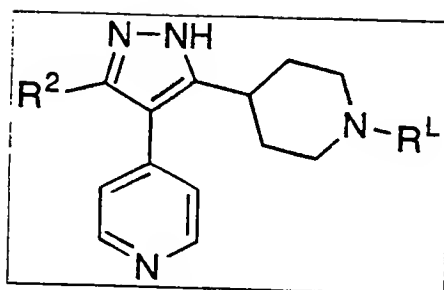
By analogy to the procedure identified above for the  
preparation of Examples B0001-B0048, the following  
15 examples B-1574 through B-2269 are prepared.

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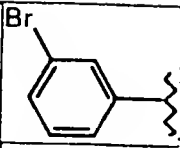
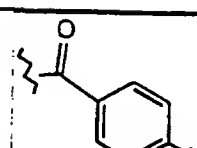
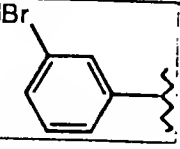
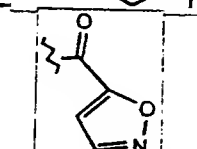
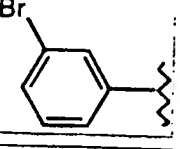
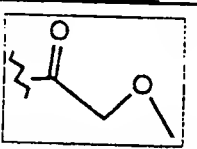
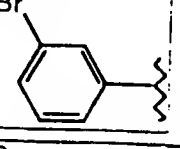
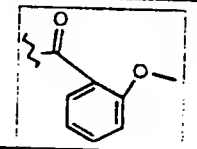
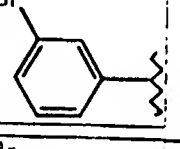
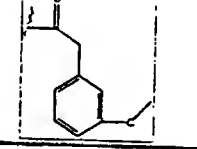
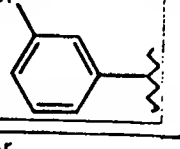
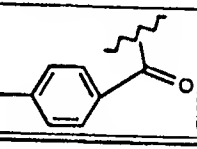
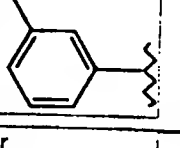
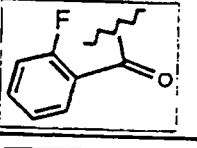
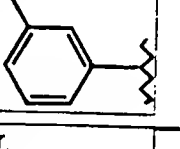
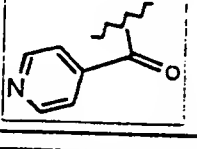
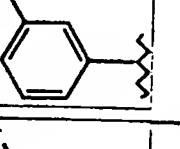
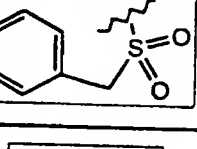
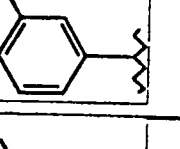
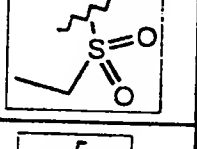

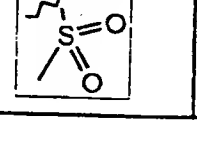
30

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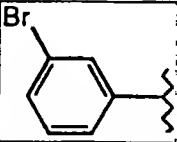
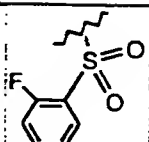
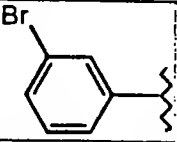
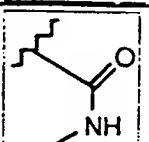
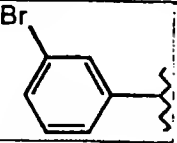
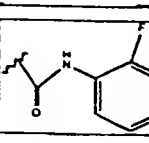
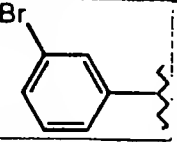
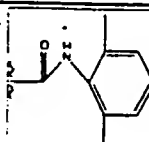
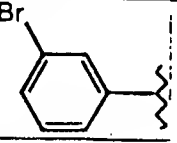
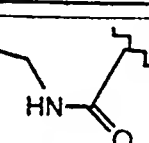
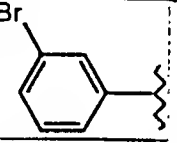
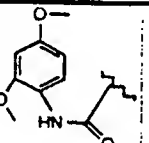


Examples B-1574 through B-1597 are prepared from Scaffold C-27

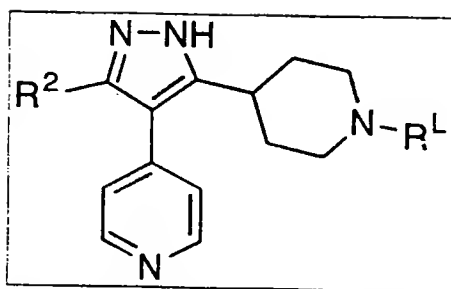
Example#	R <sup>2</sup>	R <sup>4</sup>			
B-1574					
B-1575					
B-1576					
B-1577					
B-1578					
B-1579					
B-1580					

B-1581					
B-1582					
B-1583					
B-1584					
B-1585					
B-1586					
B-1587					
B-1588					
B-1589					
B-1590					
B-1591					

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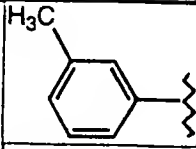
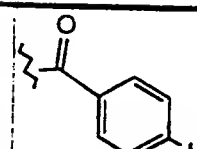
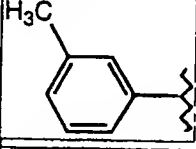
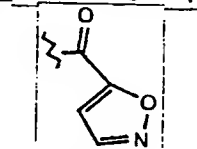
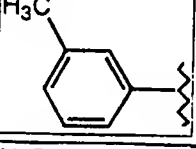
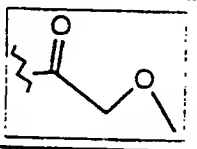
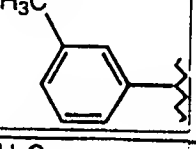
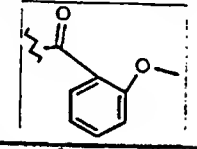
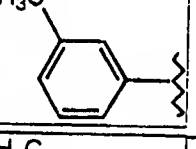
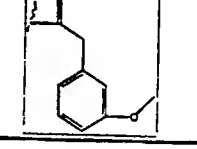
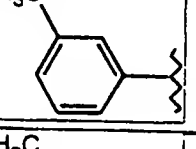
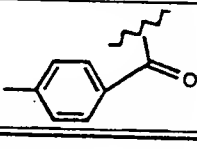
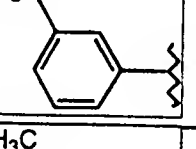
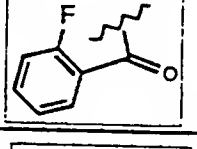
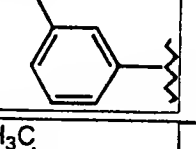
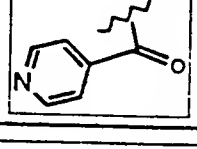
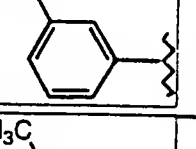
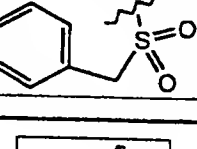
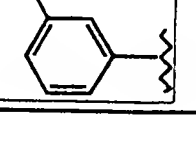
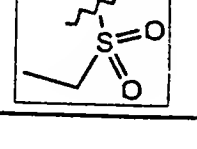
B-1592					
B-1593					
B-1594					
B-1595					
B-1596					
B-1597					

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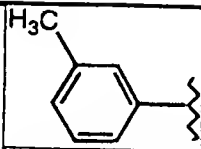
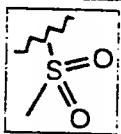
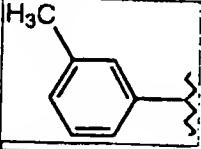
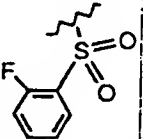
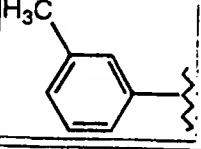
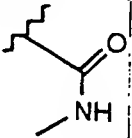
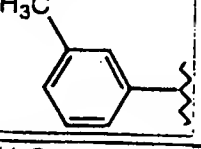
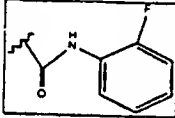
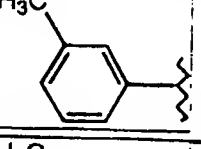
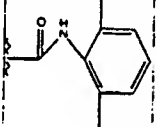
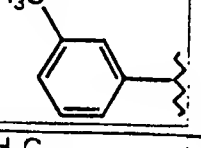
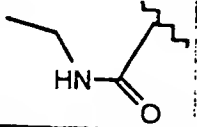
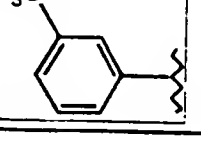
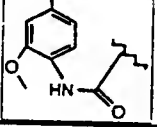


Examples B-1598 through B-1621 are prepared from Scaffold C-28

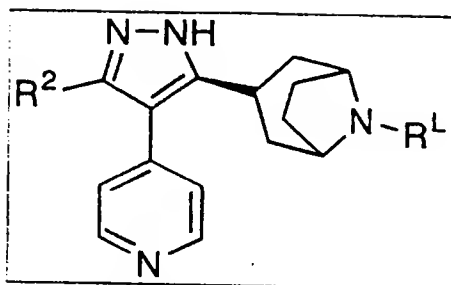
Example#	$R^2$	$R^1$			
B-1598					
B-1599					
B-1600					
B-1601					
B-1602					
B-1603					
B-1604					

Example#	R <sup>2</sup>	R <sup>L</sup>			
B-1605					
B-1606					
B-1607					
B-1608					
B-1609					
B-1610					
B-1611					
B-1612					
B-1613					
B-1614					

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Example#	R <sup>2</sup>	R <sup>L</sup>			
B-1615					
B-1616					
B-1617					
B-1618					
B-1619					
B-1620					
B-1621					

785



Examples B-1622 through B-1645 are prepared from Scaffold C-38

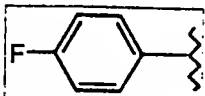
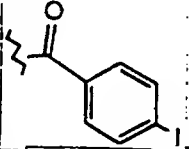
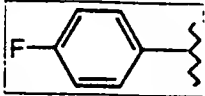
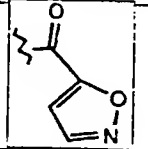
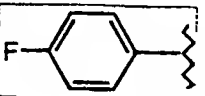
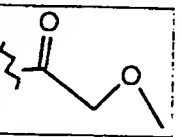
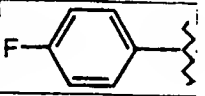
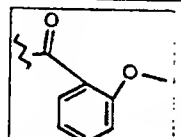
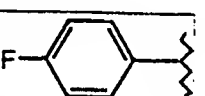
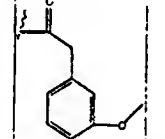
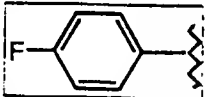
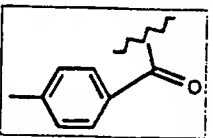
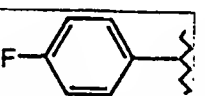
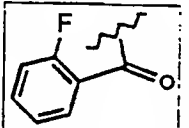
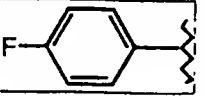
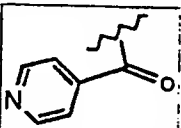
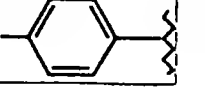
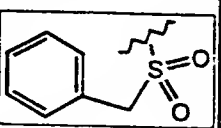
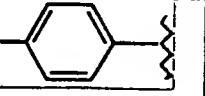
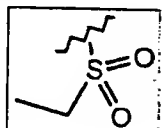
Example#

R<sup>2</sup>R<sup>4</sup>

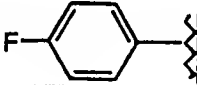
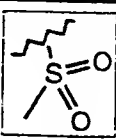
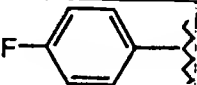
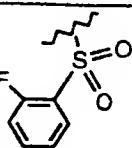
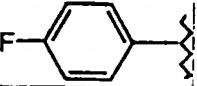
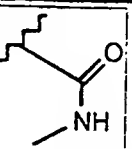
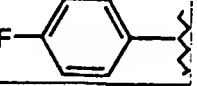
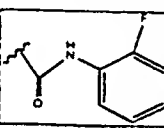
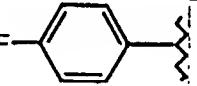
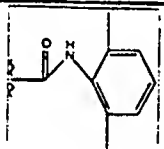
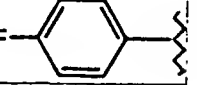
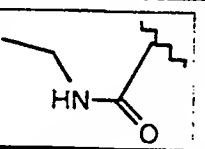
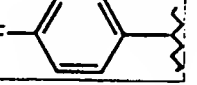
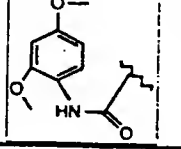
B-1622					
B-1623					
B-1624					
B-1625					
B-1626					
B-1627					
B-1628					

Example#

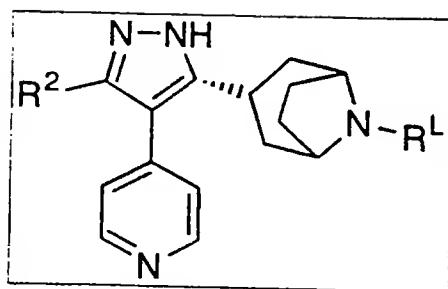
 $R^2$  $R^1$ 

B-1629					
B-1630					
B-1631					
B-1632					
B-1633					
B-1634					
B-1635					
B-1636					
B-1637					
B-1638					

Example#      R<sup>2</sup>      R<sup>L</sup>

B-1639					
B-1640					
B-1641					
B-1642					
B-1643					
B-1644					
B-1645					

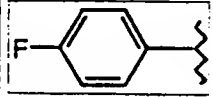
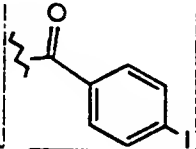
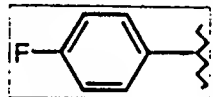
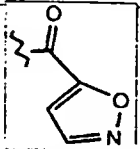
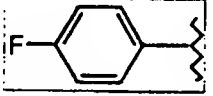
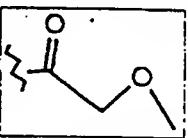
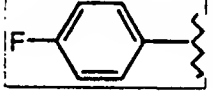
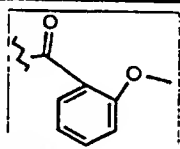
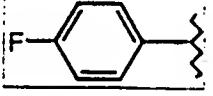
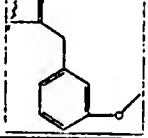
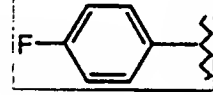
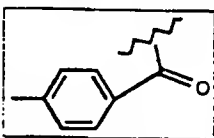
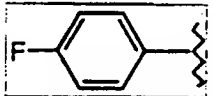
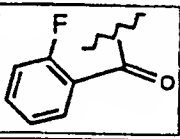
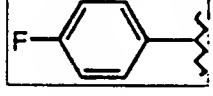
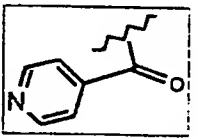
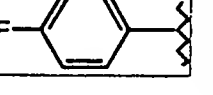
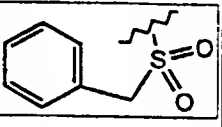
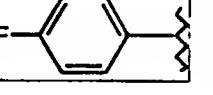
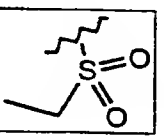
788

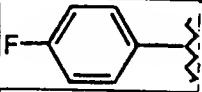
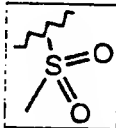
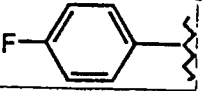
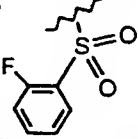
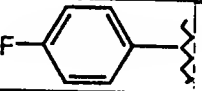
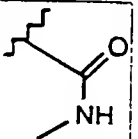
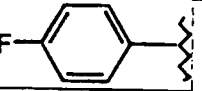
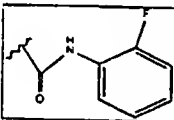
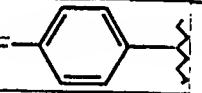
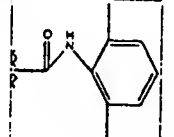
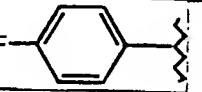
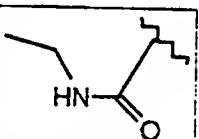
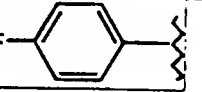
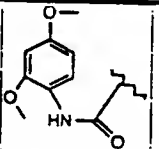


Examples B-1646 through B-1669 are prepared from Scaffold C-39

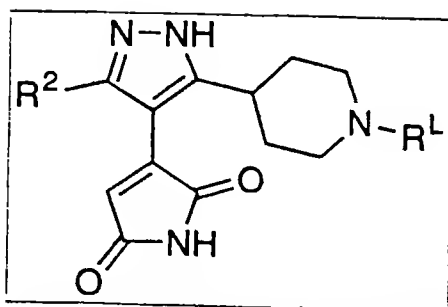
Example#	R <sup>2</sup>	R <sup>L</sup>			
B-1646					
B-1647					
B-1648					
B-1649					
B-1650					
B-1651					
B-1652					

789

Example#	R <sup>2</sup>	R <sup>L</sup>			
B-1653					
B-1654					
B-1655					
B-1656					
B-1657					
B-1658					
B-1659					
B-1660					
B-1661					
B-1662					

Example#	R <sup>2</sup>	R <sup>L</sup>			
B-1663					
B-1664					
B-1665					
B-1666					
B-1667					
B-1668					
B-1669					

791



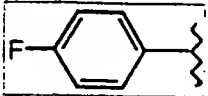
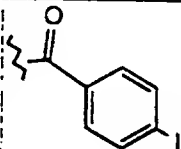
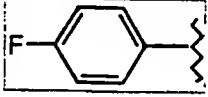
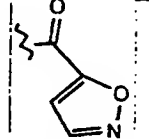
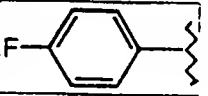
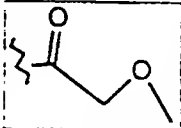
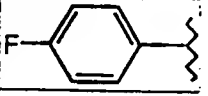
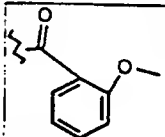
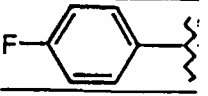
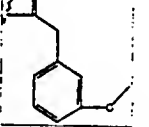
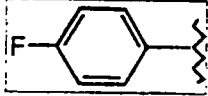
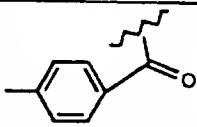
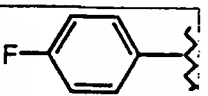
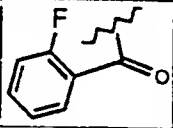
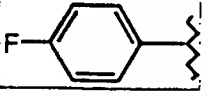
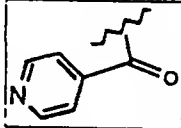
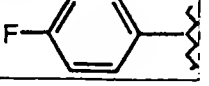
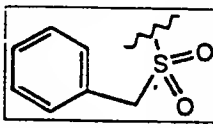
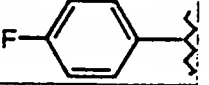
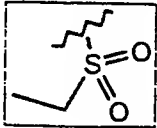
Examples B-1670 through B-1693 are prepared from Scaffold C-65

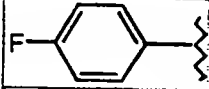
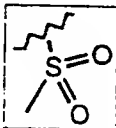
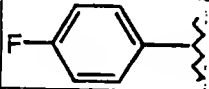
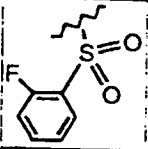
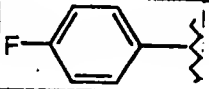
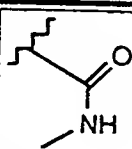
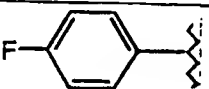
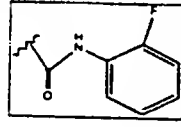
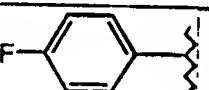
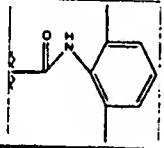
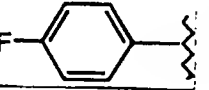
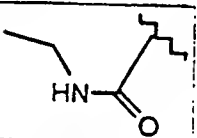
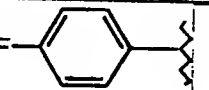
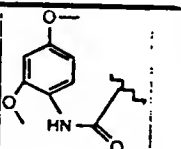
Example#	R <sup>2</sup>	R <sup>L</sup>			
B-1670					
B-1671					
B-1672					
B-1673					
B-1674					
B-1675					
B-1676					

792

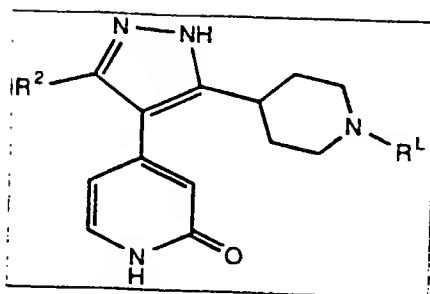
Example#

 $R^2$  $R^L$ 

B-1677					
B-1678					
B-1679					
B-1680					
B-1681					
B-1682					
B-1683					
B-1684					
B-1685					
B-1686					

Example#	R <sup>2</sup>	R <sup>1</sup>			
B-1687					
B-1688					
B-1689					
B-1690					
B-1691					
B-1692					
B-1693					

794

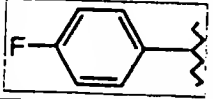
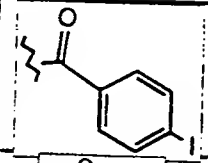
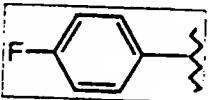
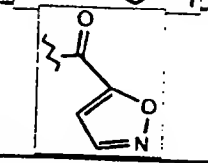
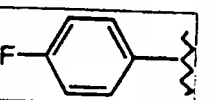
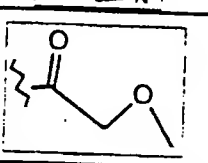
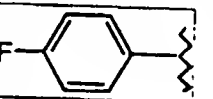
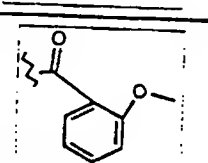
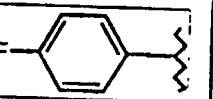
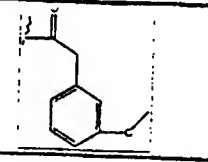
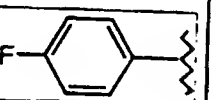
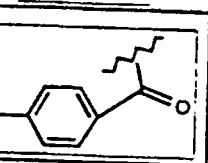
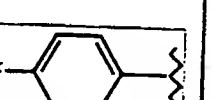
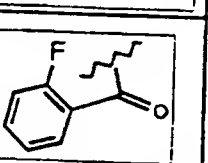
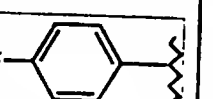
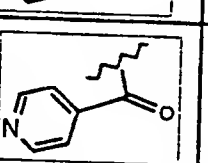
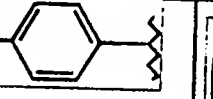
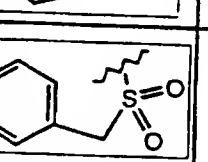
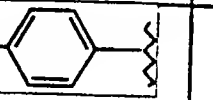
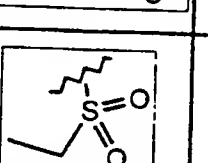


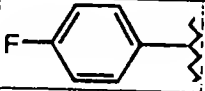
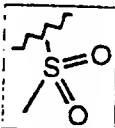
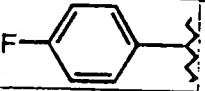
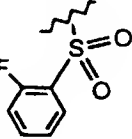
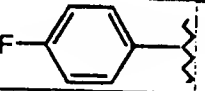
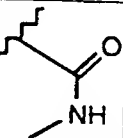
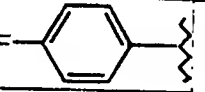
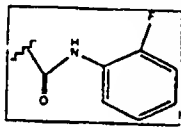
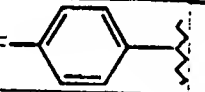
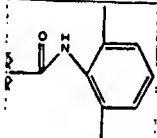
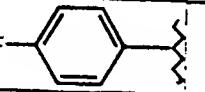
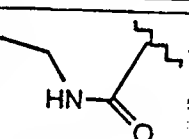
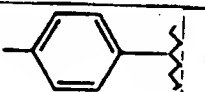
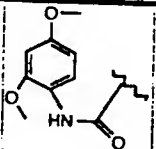
Examples B-1694 through B-1717 are prepared from Scaffold C-66

Example#	$R^2$	$R^L$			
B-1694					
B-1695					
B-1696					
B-1697					
B-1698					
B-1699					
B-1700					

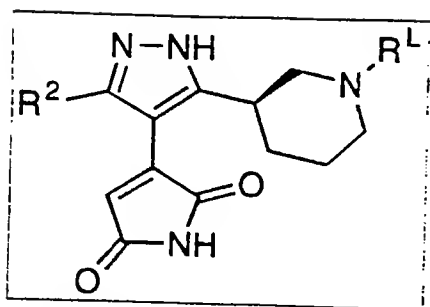
Example#

 $R^2$  $R^1$ 

B-1701					
B-1702					
B-1703					
B-1704					
B-1705					
B-1706					
B-1707					
B-1708					
B-1709					
B-1710					

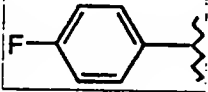
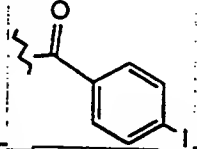
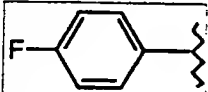
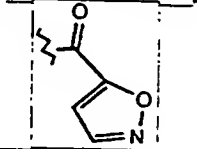
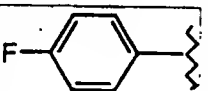
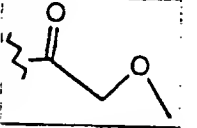
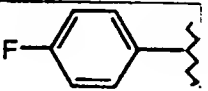
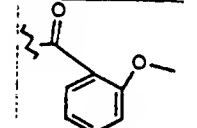
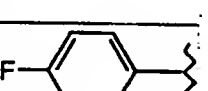
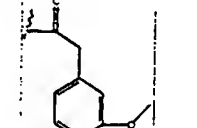
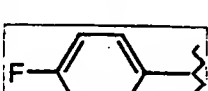
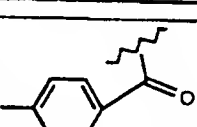

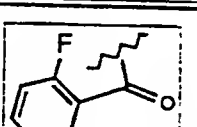
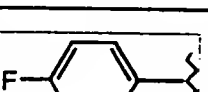
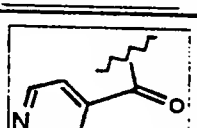
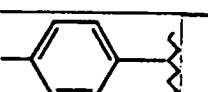
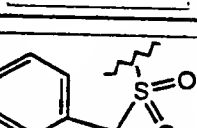
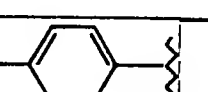
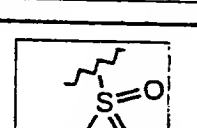
Example#	R <sup>2</sup>	R <sup>1</sup>			
B-1711					
B-1712					
B-1713					
B-1714					
B-1715					
B-1716					
B-1717					

797



Examples B-1718 through B-1741 are prepared from Scaffold C-69

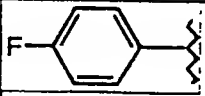
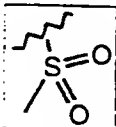
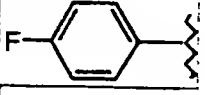
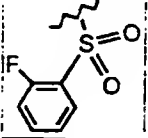
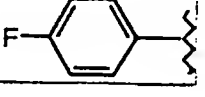
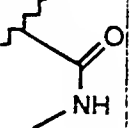
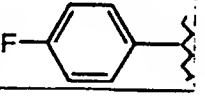
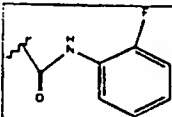
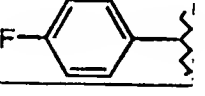
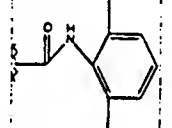
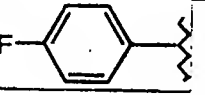
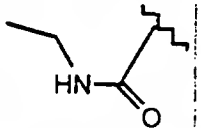
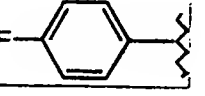
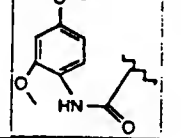
Example#	R <sup>2</sup>	R <sup>L</sup>			
B-1718					
B-1719					
B-1720					
B-1721					
B-1722					
B-1723					
B-1724					

Example#	R <sup>2</sup>	R <sup>L</sup>			
B-1725					
B-1726					
B-1727					
B-1728					
B-1729					
B-1730					
B-1731					
B-1732					
B-1733					
B-1734					

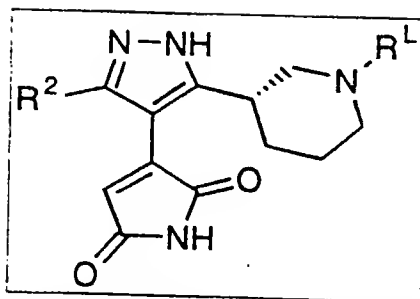
799

Example#

 $R^2$  $R^L$ 

B-1735					
B-1736					
B-1737					
B-1738					
B-1739					
B-1740					
B-1741					

800



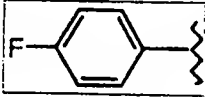
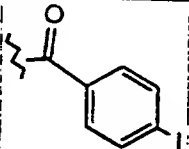
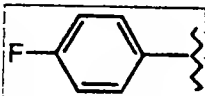
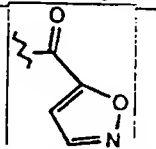
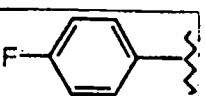
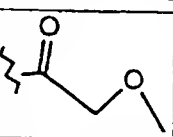
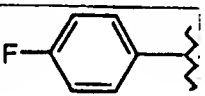
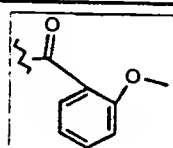
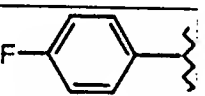
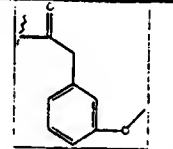
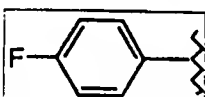
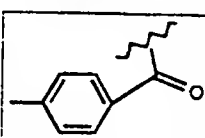
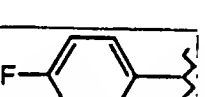
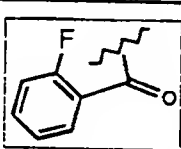
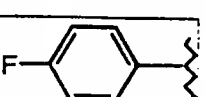
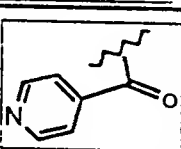
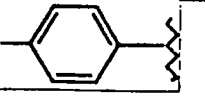
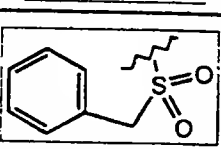
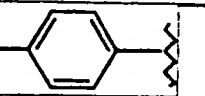
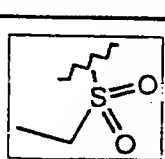
Examples B-1742 through B-1765 are prepared from Scaffold C-70

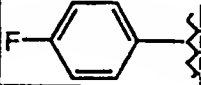
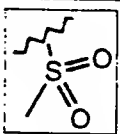
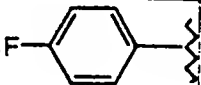
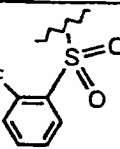
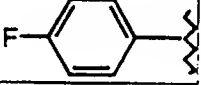
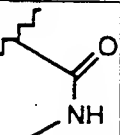
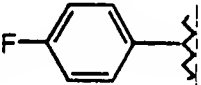
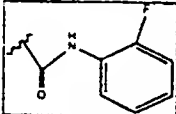
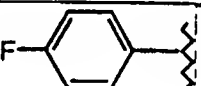
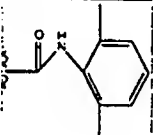
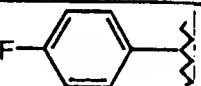
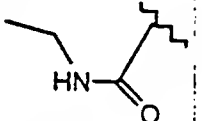
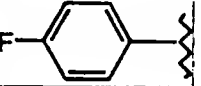
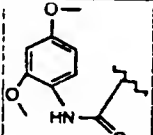
Example#	R <sup>2</sup>	R <sup>L</sup>			
B-1742					
B-1743					
B-1744					
B-1745					
B-1746					
B-1747					
B-1748					

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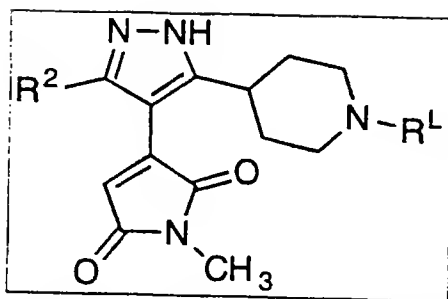
Example#

 $R^2$  $R^L$ 

B-1749					
B-1750					
B-1751					
B-1752					
B-1753					
B-1754					
B-1755					
B-1756					
B-1757					
B-1758					

Example#	R <sup>2</sup>	R <sup>L</sup>			
B-1759					
B-1760					
B-1761					
B-1762					
B-1763					
B-1764					
B-1765					

803

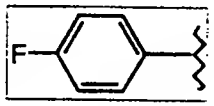
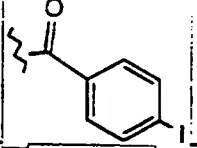
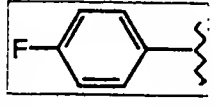
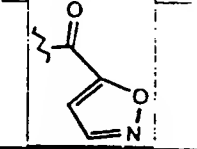
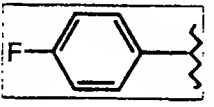
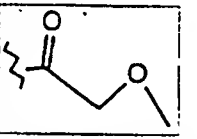
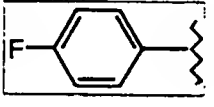
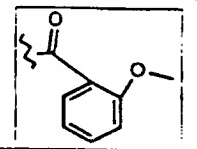
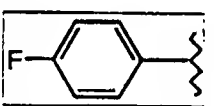
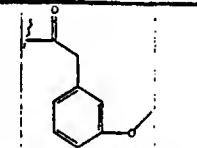
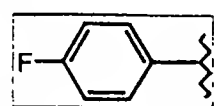
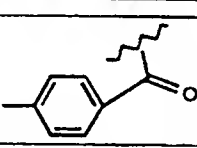
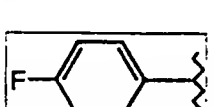
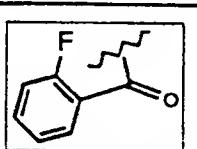
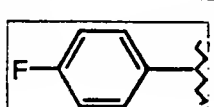
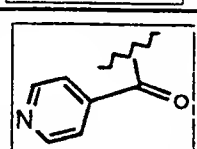
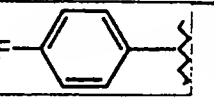
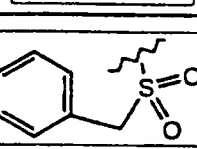
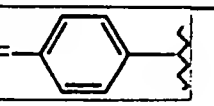
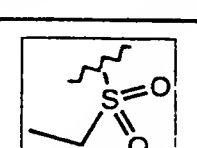


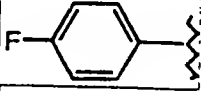
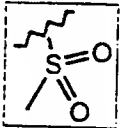
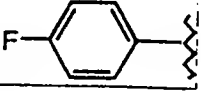
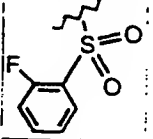
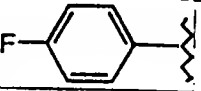
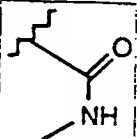
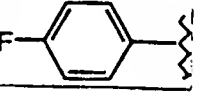
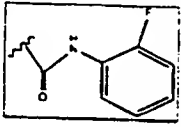
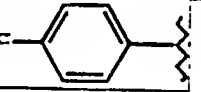
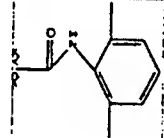
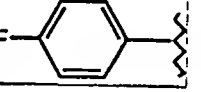
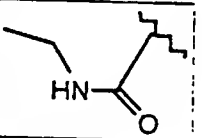
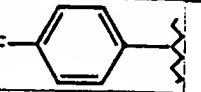
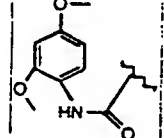
Examples B-1766 through B-1789 are prepared from Scaffold C-71

Example#	$R^2$	$R^L$			
B-1766					
B-1767					
B-1768					
B-1769					
B-1770					
B-1771					
B-1772					

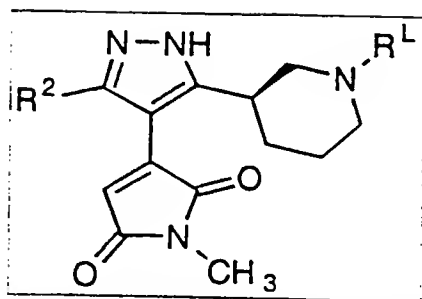
Example#

 $R^2$  $R^L$ 

B-1773					
B-1774					
B-1775					
B-1776					
B-1777					
B-1778					
B-1779					
B-1780					
B-1781					
B-1782					

Example#	R <sup>2</sup>	R <sup>1</sup>			
B-1783					
B-1784					
B-1785					
B-1786					
B-1787					
B-1788					
B-1789					

806



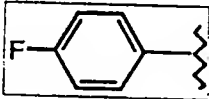
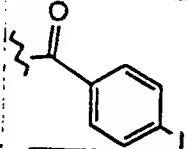
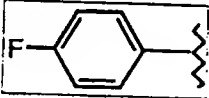
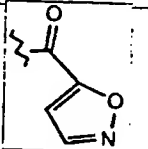
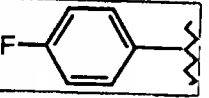
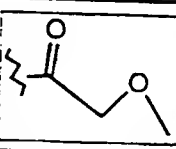
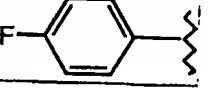
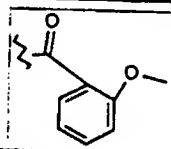
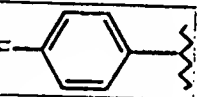
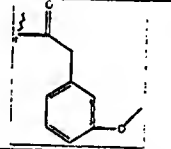
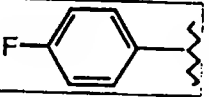
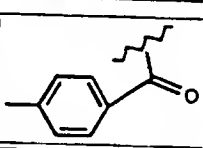
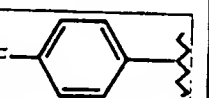
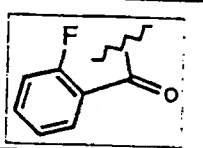
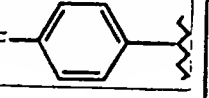
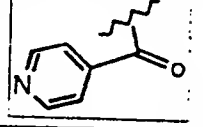
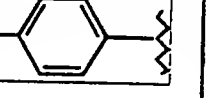
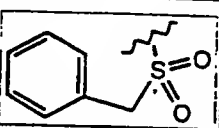
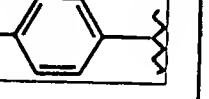
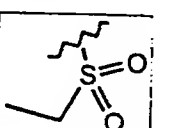
Examples B-1790 through B-1813 are prepared from Scaffold C-72

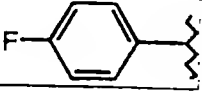
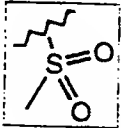
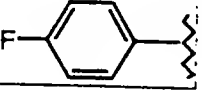
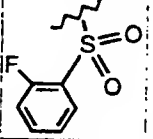
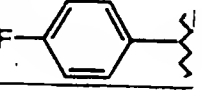
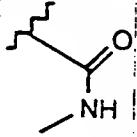
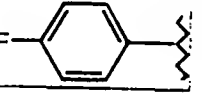
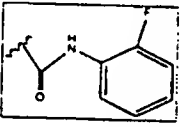
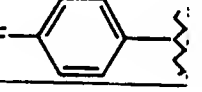
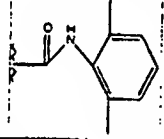
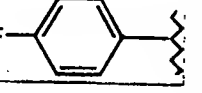
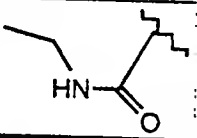
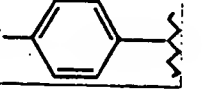
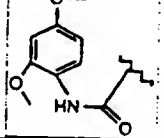
Example#

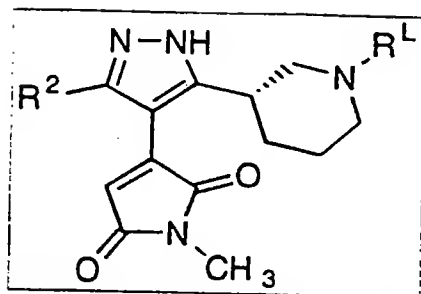
 $R^2$  $R^L$ 

B-1790					
B-1791					
B-1792					
B-1793					
B-1794					
B-1795					
B-1796					

807

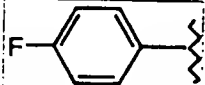
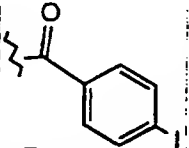
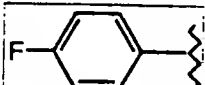
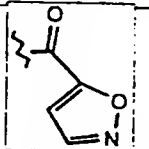
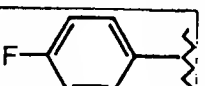
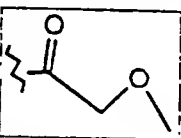
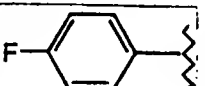
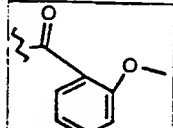
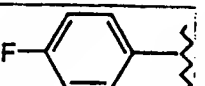
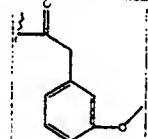
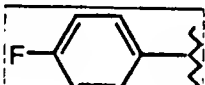
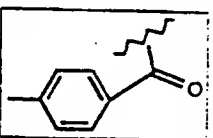
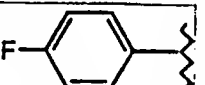
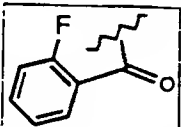
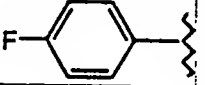
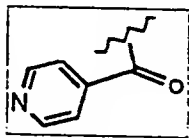
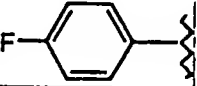
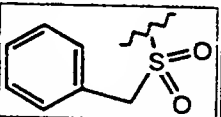
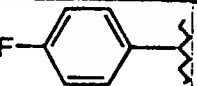
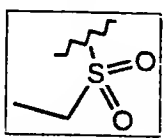
Example#	R <sup>2</sup>	R <sup>L</sup>			
B-1797					
B-1798					
B-1799					
B-1800					
B-1801					
B-1802					
B-1803					
B-1804					
B-1805					
B-1806					

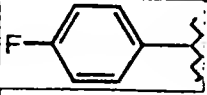
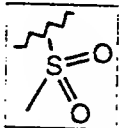
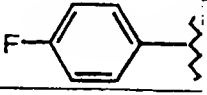
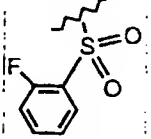
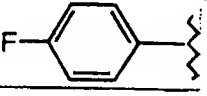
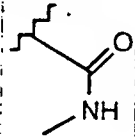
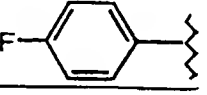
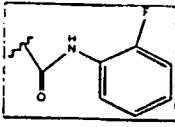
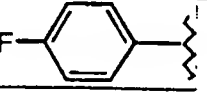
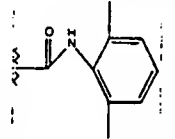
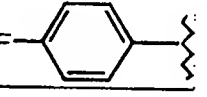
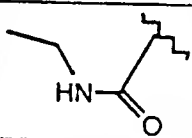
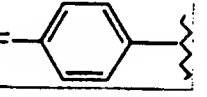
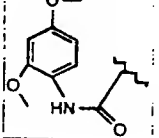
Example#	R <sup>2</sup>	R <sup>L</sup>			
B-1807					
B-1808					
B-1809					
B-1810					
B-1811					
B-1812					
B-1813					

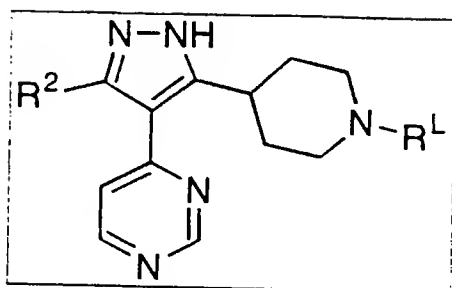


Examples B-1814 through B-1837 are prepared from Scaffold C-73

Example#	R <sup>2</sup>	R <sup>1</sup>			
B-1814					
B-1815					
B-1816					
B-1817					
B-1818					
B-1819					
B-1820					

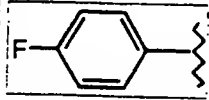
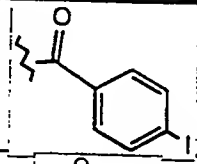
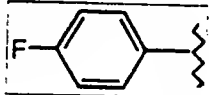
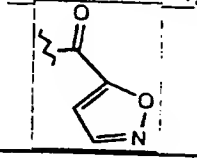
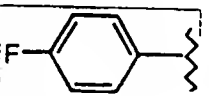
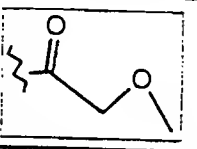
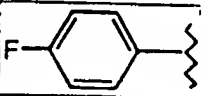
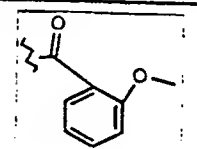
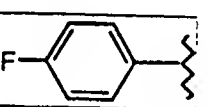
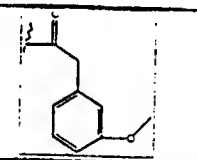
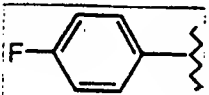
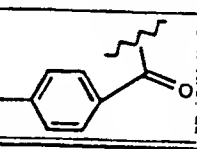
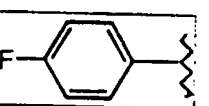
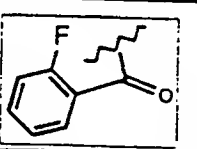
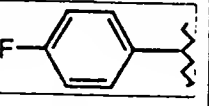
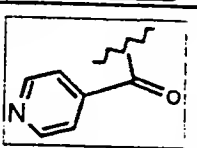
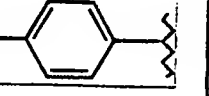
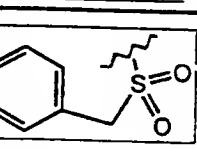
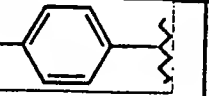
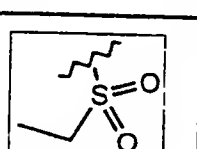
Example#	R <sup>2</sup>	R <sup>1</sup>			
B-1821					
B-1822					
B-1823					
B-1824					
B-1825					
B-1826					
B-1827					
B-1828					
B-1829					
B-1830					

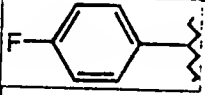
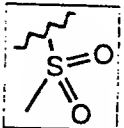
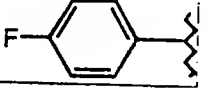
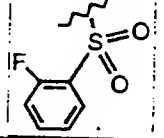
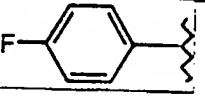
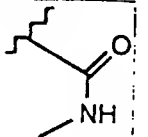
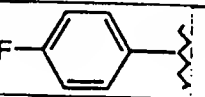
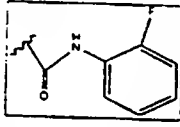
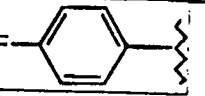
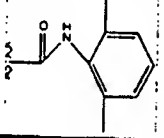
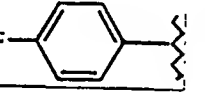
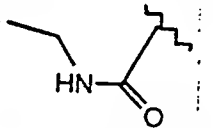
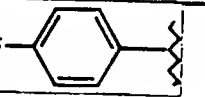
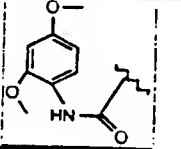
Example#	R <sup>2</sup>	R <sup>1</sup>			
B-1831					
B-1832					
B-1833					
B-1834					
B-1835					
B-1836					
B-1837					



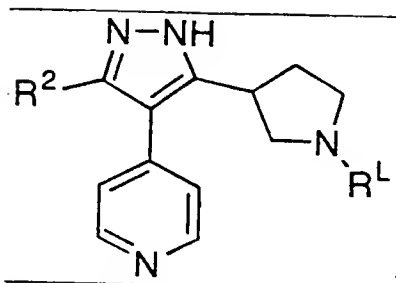
Examples B-1838 through B-1861 are prepared from Scaffold C-33

Example#	R <sup>2</sup>	R <sup>L</sup>			
B-1838					
B-1839					
B-1840					
B-1841					
B-1842					
B-1843					
B-1844					

Example#	R <sup>2</sup>	R <sup>L</sup>			
B-1845					
B-1846					
B-1847					
B-1848					
B-1849					
B-1850					
B-1851					
B-1852					
B-1853					
B-1854					

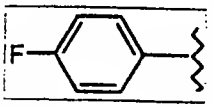
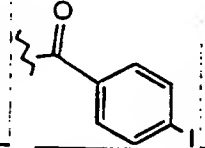
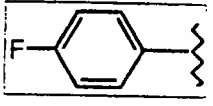
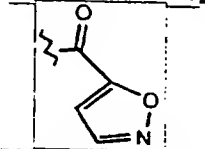
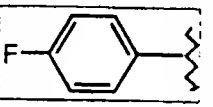
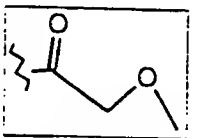
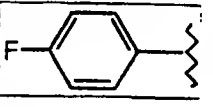
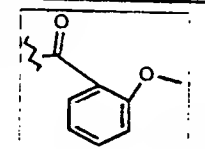
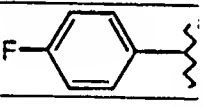
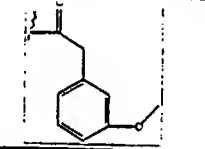
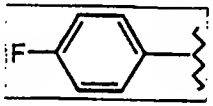
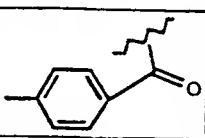
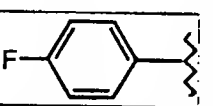
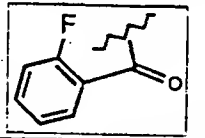
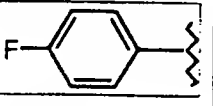
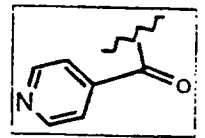
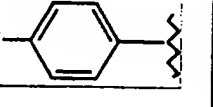
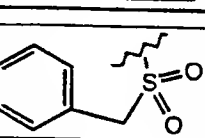
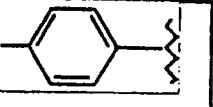
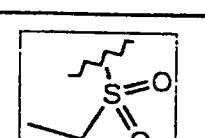
Example#	R <sup>2</sup>	R <sup>L</sup>			
B-1855					
B-1856					
B-1857					
B-1858					
B-1859					
B-1860					
B-1861					

815



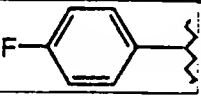
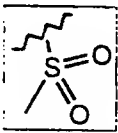
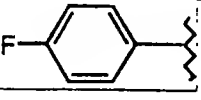
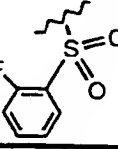
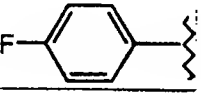
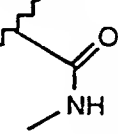
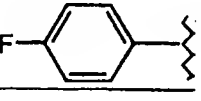
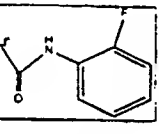
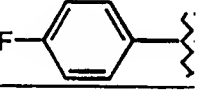
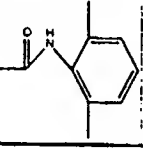
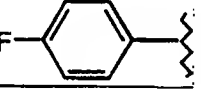
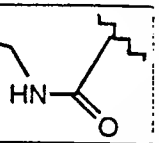
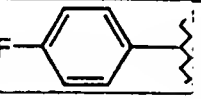
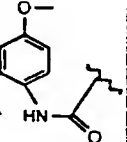
Examples B-1862 through B-1885 are prepared from Scaffold C-45

Example#	R <sup>2</sup>	R <sup>4</sup>			
B-1862					
B-1863					
B-1864					
B-1865					
B-1866					
B-1867					
B-1868					

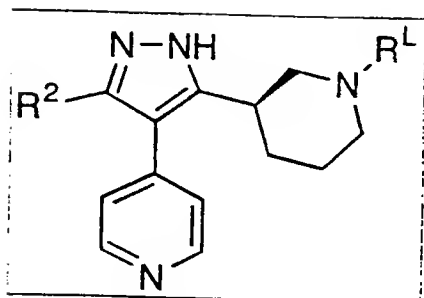
Example#	R <sup>2</sup>	R <sup>L</sup>			
B-1869					
B-1870					
B-1871					
B-1872					
B-1873					
B-1874					
B-1875					
B-1876					
B-1877					
B-1878					

Example#

 $R^2$  $R^L$ 

B-1879					
B-1880					
B-1881					
B-1882					
B-1883					
B-1884					
B-1885					

818

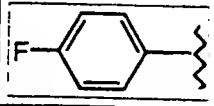
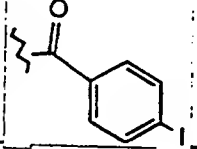
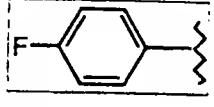
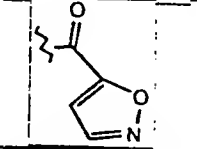
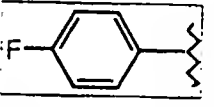
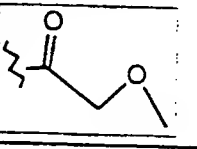
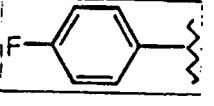
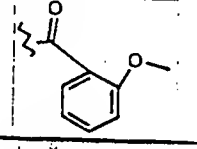
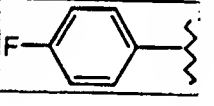
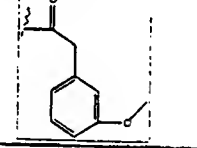
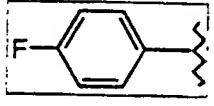
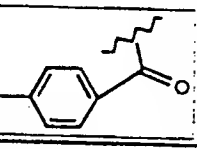
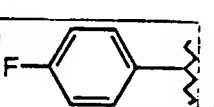
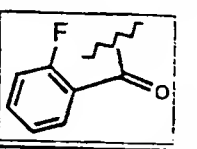
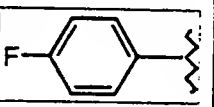
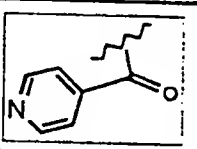
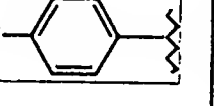
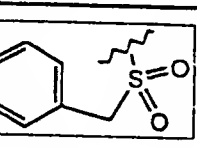
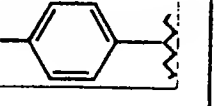
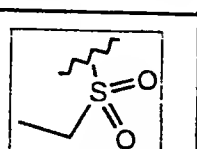


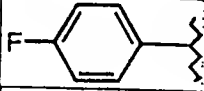
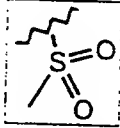
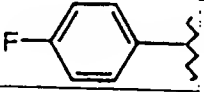
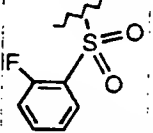
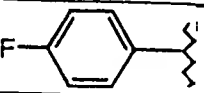
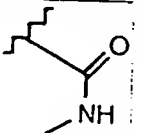
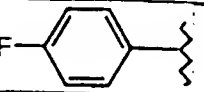
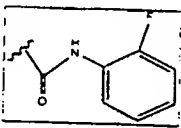
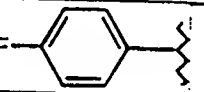
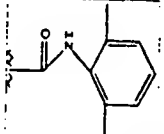
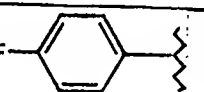
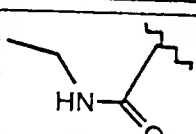
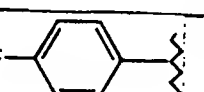
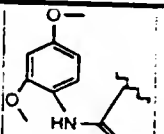
Examples B-1886 through B-1909 prepared from Scaffold C-42

Example#	R <sup>2</sup>	R <sup>L</sup>			
B-1886					
B-1887					
B-1888					
B-1889					
B-1890					
B-1891					
B-1892					

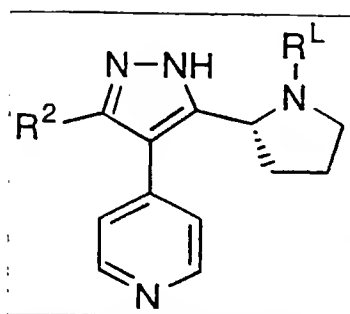
Example#

 $R^2$  $R^L$ 

B-1893					
B-1894					
B-1895					
B-1896					
B-1897					
B-1898					
B-1899					
B-1900					
B-1901					
B-1902					

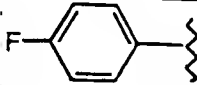
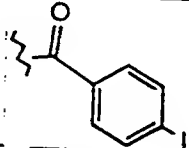
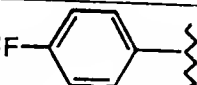
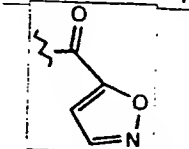
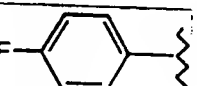
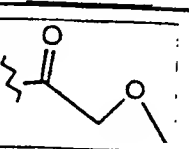
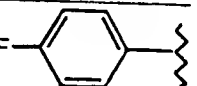
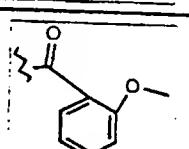
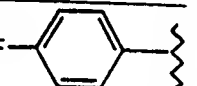
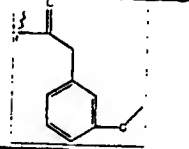
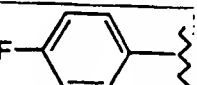
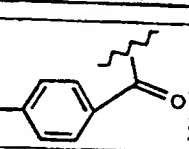
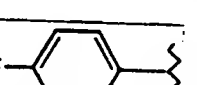
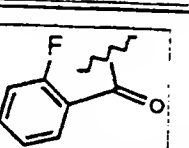
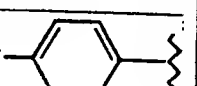
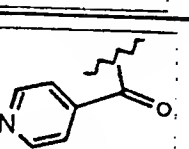
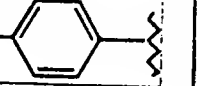
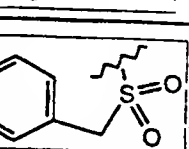
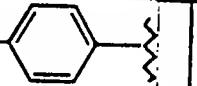
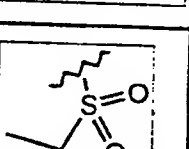
Example#	R <sup>2</sup>	R <sup>1</sup>			
B-1903					
B-1904					
B-1905					
B-1906					
B-1907					
B-1908					
B-1909					

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Examples B-1910 through B-1933 are prepared from Scaffold C-44

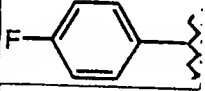
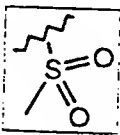
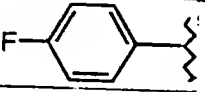
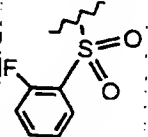
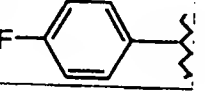
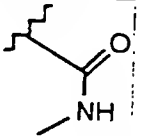
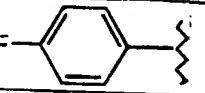
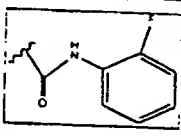
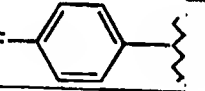
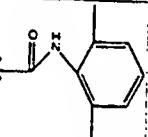
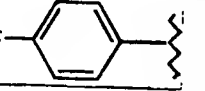
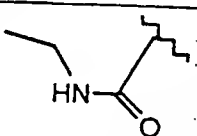
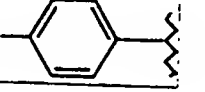
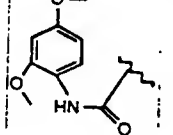
Example#	R <sup>2</sup>	R <sup>L</sup>			
B-1910					
B-1911					
B-1912					
B-1913					
B-1914					
B-1915					
B-1916					

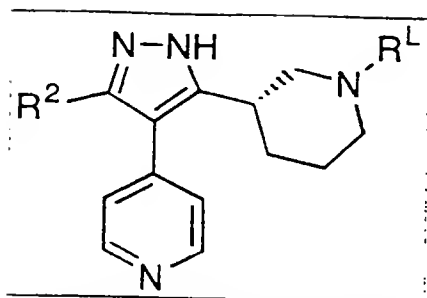
Example#	R <sup>2</sup>	R <sup>L</sup>			
B-1917					
B-1918					
B-1919					
B-1920					
B-1921					
B-1922					
B-1923					
B-1924					
B-1925					
B-1926					

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Example#

 $R^2$  $R^L$ 


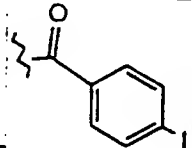

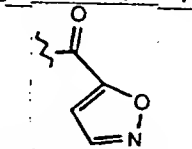
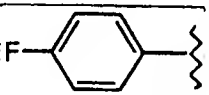
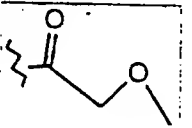
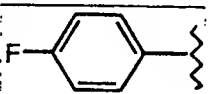
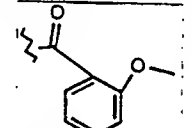
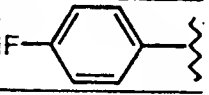
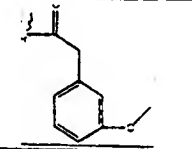
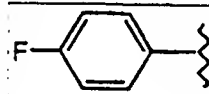
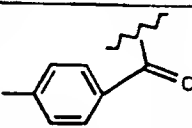
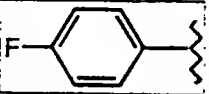
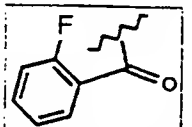

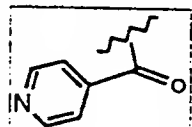
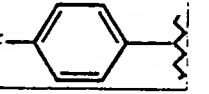
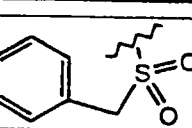
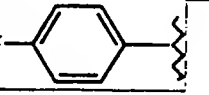
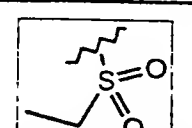
B-1927					
B-1928					
B-1929					
B-1930					
B-1931					
B-1932					
B-1933					

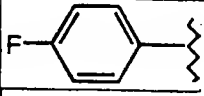
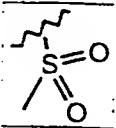
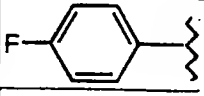
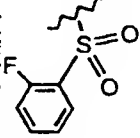
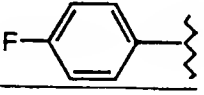
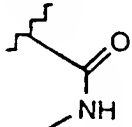
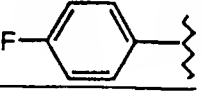
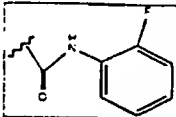
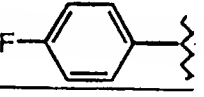
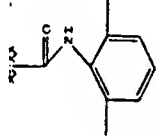
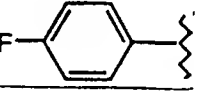
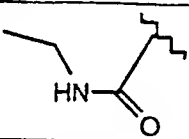
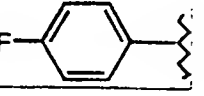
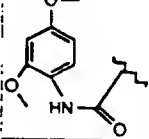


Examples B-1934 through B-1957 are prepared from Scaffold C-41

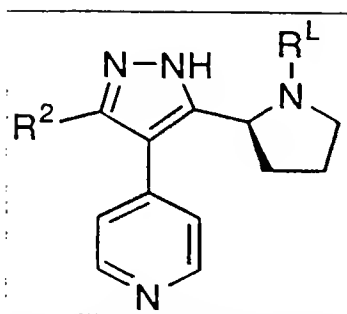
Example#	R <sup>2</sup>	R <sup>L</sup>			
B-1934					
B-1935					
B-1936					
B-1937					
B-1938					
B-1939					
B-1940					

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Example#	R <sup>2</sup>	R <sup>1</sup>			
B-1941					
B-1942					
B-1943					
B-1944					
B-1945					
B-1946					
B-1947					
B-1948					
B-1949					
B-1950					


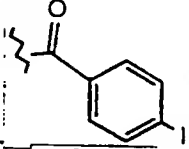
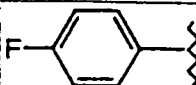
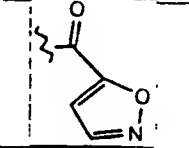
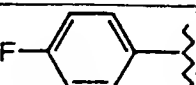
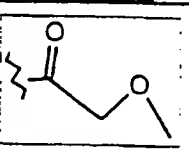
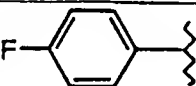
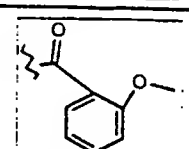
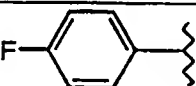
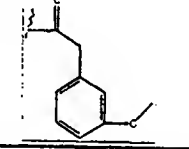
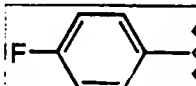
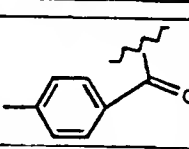
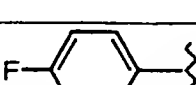
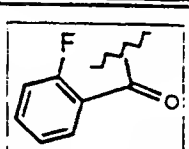
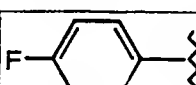
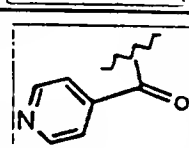
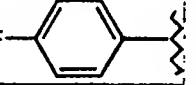
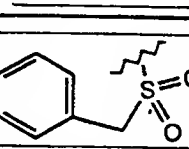
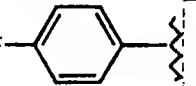
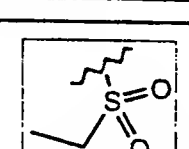
Example#	R <sup>2</sup>	R <sup>L</sup>			
B-1951					
B-1952					
B-1953					
B-1954					
B-1955					
B-1956					
B-1957					

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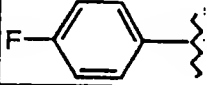
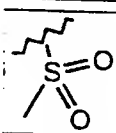
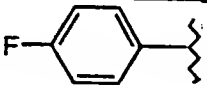
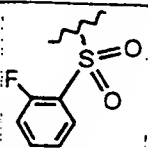
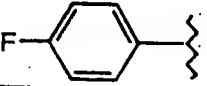
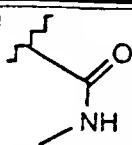
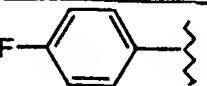
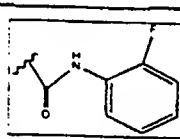
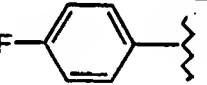
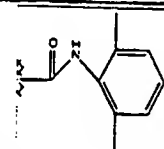
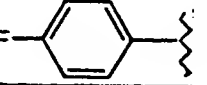
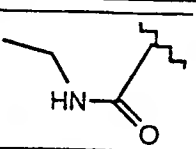
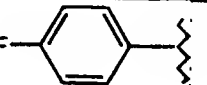
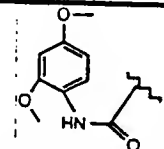
Examples B-1958 through B-1981 are prepared from Scaffold C-43

Example#	$R^2$	$R^L$			
B-1958					
B-1959					
B-1960					
B-1961					
B-1962					
B-1963					
B-1964					

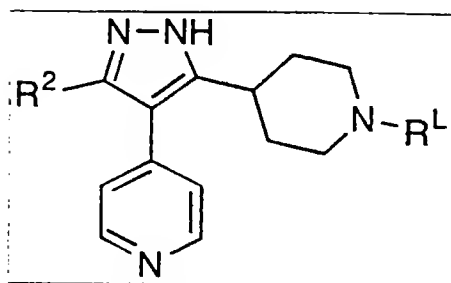
Example#	R <sup>2</sup>	R <sup>L</sup>			
B-1965					
B-1966					
B-1967					
B-1968					
B-1969					
B-1970					
B-1971					
B-1972					
B-1973					
B-1974					

Example#

 $R^2$  $R^1$ 

B-1975					
B-1976					
B-1977					
B-1978					
B-1979					
B-1980					
B-1981					

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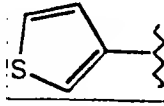
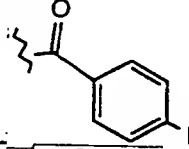
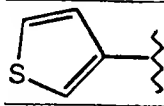
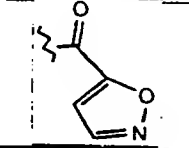
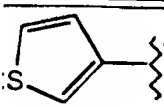
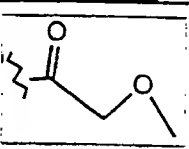
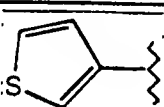
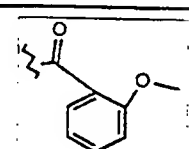
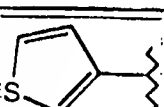
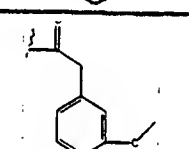
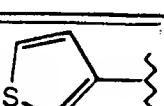
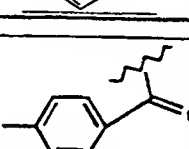
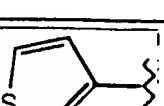
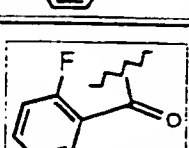
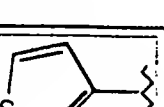
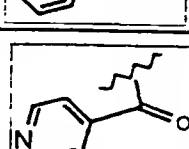
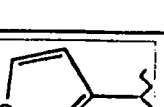
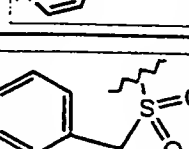

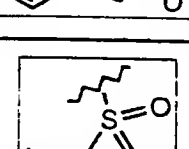


Examples B-1982 through B-2005 are prepared from Scaffold C-30

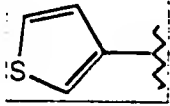
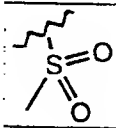
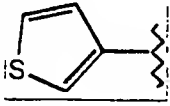
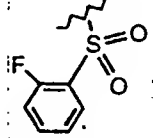
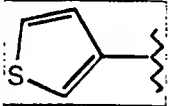
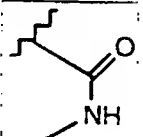
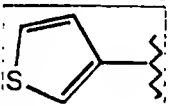
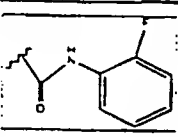
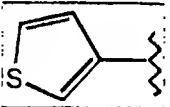
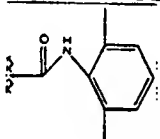
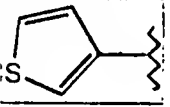
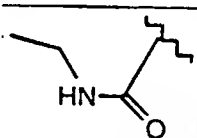
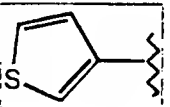
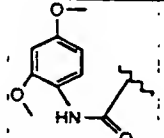
Example#

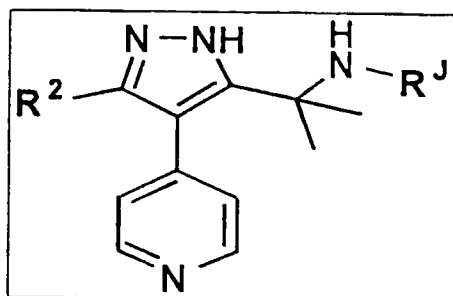
R<sup>2</sup>R<sup>L</sup>

B-1982					
B-1983					
B-1984					
B-1985					
B-1986					
B-1987					
B-1988					

Example#	R <sup>2</sup>	R <sup>L</sup>			
B-1989					
B-1990					
B-1991					
B-1992					
B-1993					
B-1994					
B-1995					
B-1996					
B-1997					
B-1998					

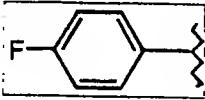
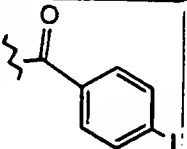
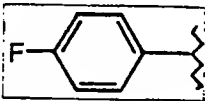
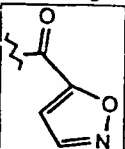
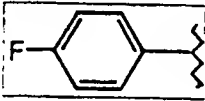
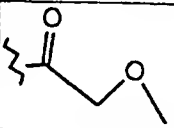
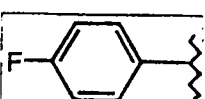
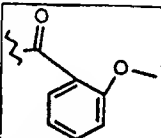
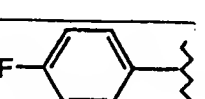
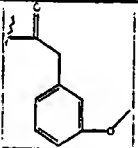
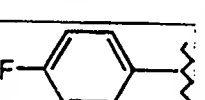
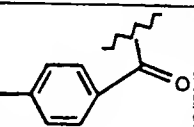
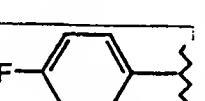
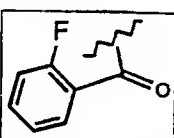
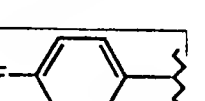
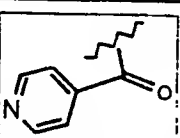
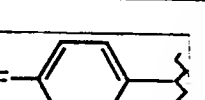
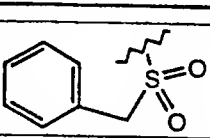
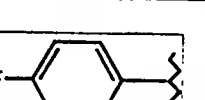
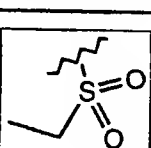
832

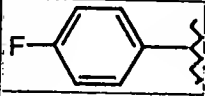
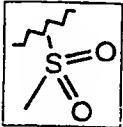
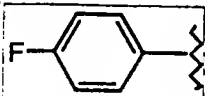
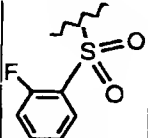
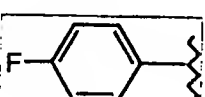
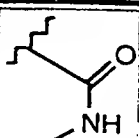
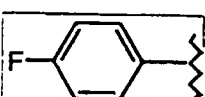
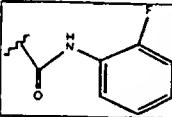
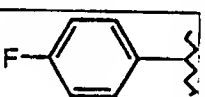
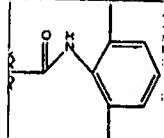
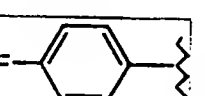
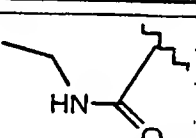
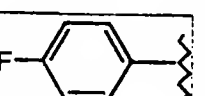
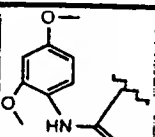
Example#	R <sup>2</sup>	R <sup>L</sup>			
B-1999					
B-2000					
B-2001					
B-2002					
B-2003					
B-2004					
B-2005					



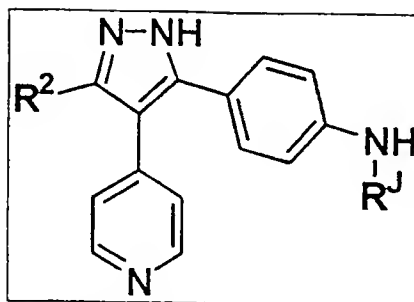
Examples B-2006 through B-2029 are prepared from Scaffold C-60

Example#	R <sup>2</sup>	R <sup>J</sup>			
B-2006					
B-2007					
B-2008					
B-2009					
B-2010					
B-2011					
B-2012					

Example#	R <sup>2</sup>	R <sup>1</sup>			
B-2013					
B-2014					
B-2015					
B-2016					
B-2017					
B-2018					
B-2019					
B-2020					
B-2021					
B-2022					

Example#	R <sup>2</sup>	R <sup>J</sup>			
B-2023					
B-2024					
B-2025					
B-2026					
B-2027					
B-2028					
B-2029					

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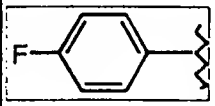
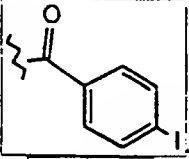
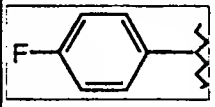
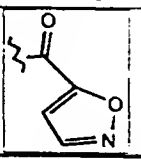
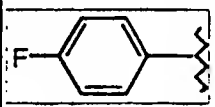
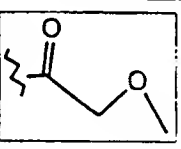
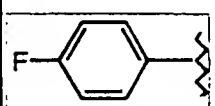
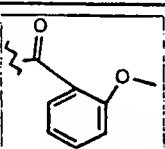
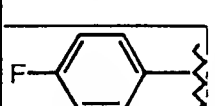
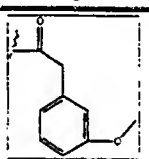
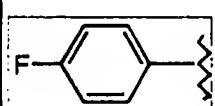
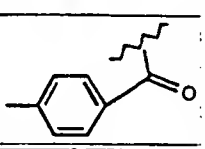
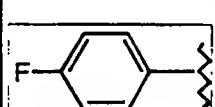
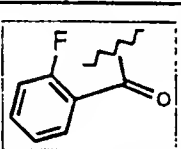
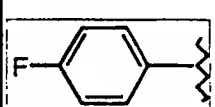
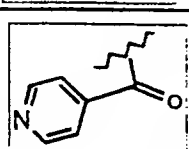
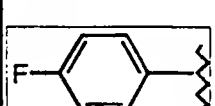
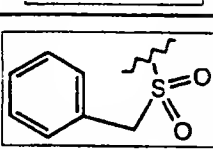
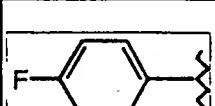
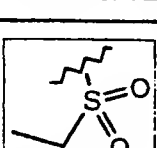


Examples B-2030 through B-2053 are prepared from Scaffold C-36

Example#	$R^2$	$R^1$			
B-2030					
B-2031					
B-2032					
B-2033					
B-2034					
B-2035					
B-2036					

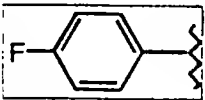
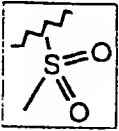
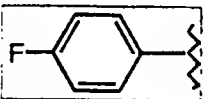
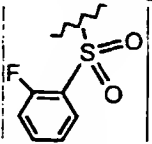
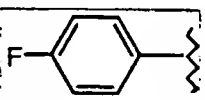
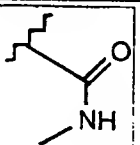
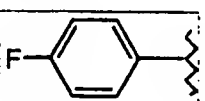
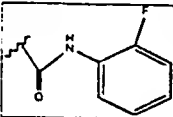
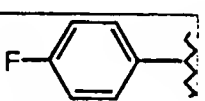
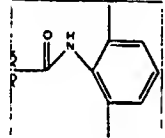
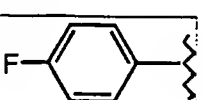
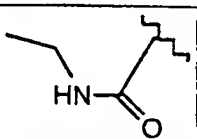
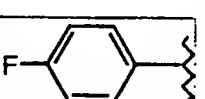
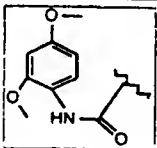
Example#

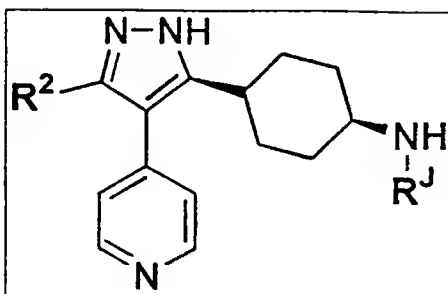
 $R^2$  $R^J$ 

B-2037					
B-2038					
B-2039					
B-2040					
B-2041					
B-2042					
B-2043					
B-2044					
B-2045					
B-2046					

Example#

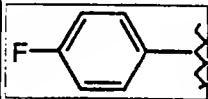
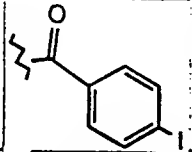
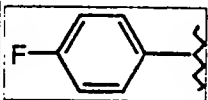
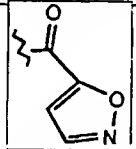
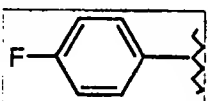
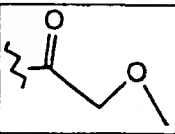
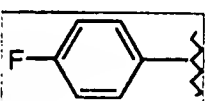
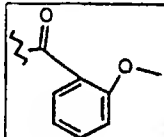
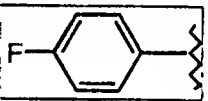
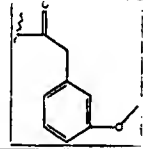
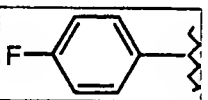
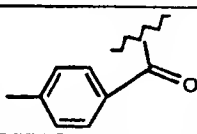
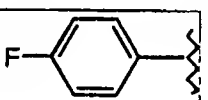
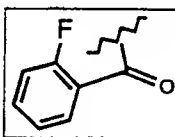
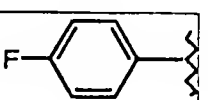
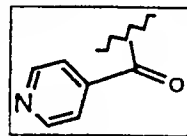
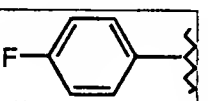
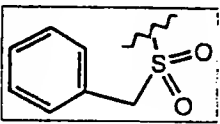
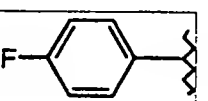
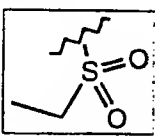
 $R^2$  $R^1$ 

B-2047					
B-2048					
B-2049					
B-2050					
B-2051					
B-2052					
B-2053					

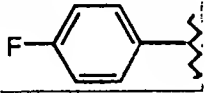
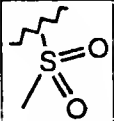
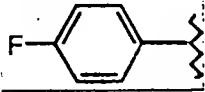
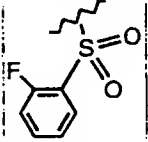
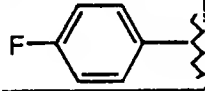
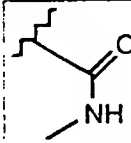
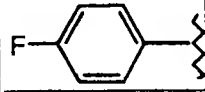
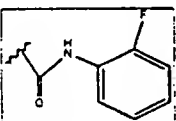

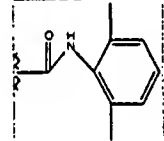

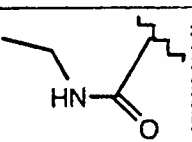
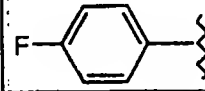
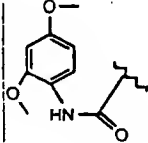


Examples B-2054 through B-2077 are prepared from Scaffold C-34

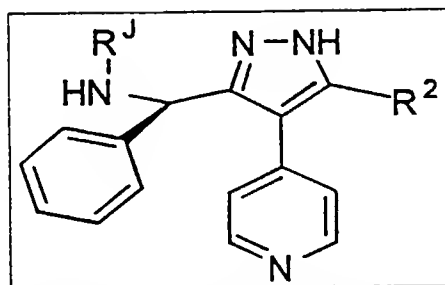
Example#	R <sup>2</sup>	R <sup>J</sup>			
B-2054					
B-2055					
B-2056					
B-2057					
B-2058					
B-2059					
B-2060					

Example#	R <sup>2</sup>	R <sup>1</sup>			
B-2061					
B-2062					
B-2063					
B-2064					
B-2065					
B-2066					
B-2067					
B-2068					
B-2069					
B-2070					

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Example#	R <sup>2</sup>	R <sup>1</sup>			
B-2071					
B-2072					
B-2073					
B-2074					
B-2075					
B-2076					
B-2077					

842



Examples B-2078 through B-2101 are prepared from Scaffold C-57

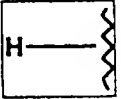
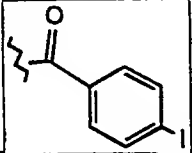
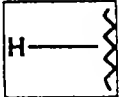
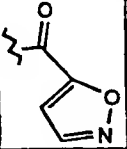
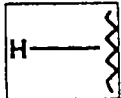
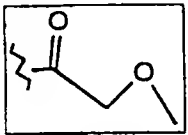
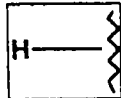
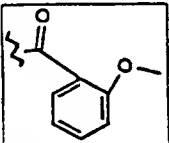
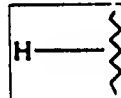
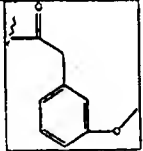
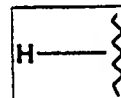
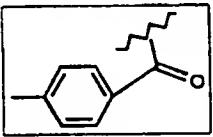
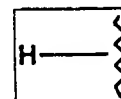
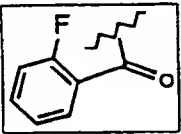
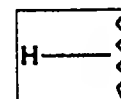
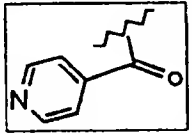
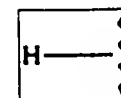
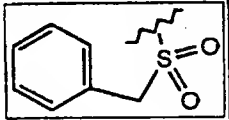
Example#

 $R^2$  $R^J$ 

B-2078					
B-2079					
B-2080					
B-2081					
B-2082					
B-2083					
B-2084					

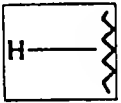
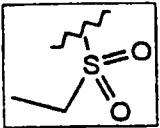
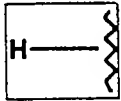
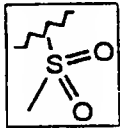
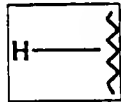
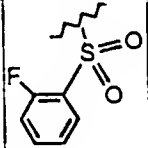
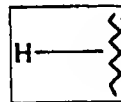
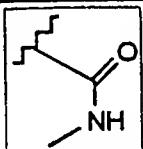
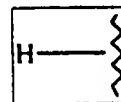
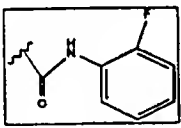
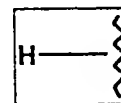
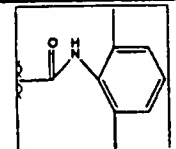
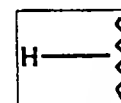
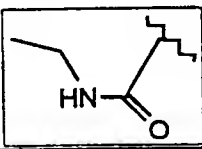
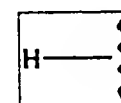
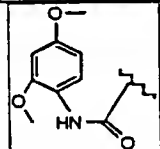
Example#

 $R^2$  $R^1$ 

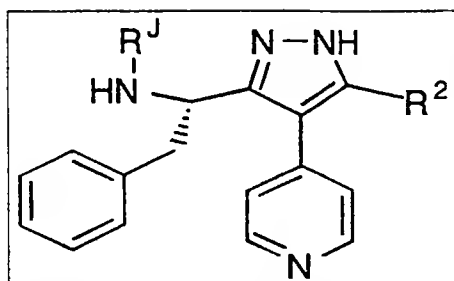
B-2085					
B-2086					
B-2087					
B-2088					
B-2089					
B-2090					
B-2091					
B-2092					
B-2093					

Example#

 $R^2$  $R^1$ 

B-2094					
B-2095					
B-2096					
B-2097					
B-2098					
B-2099					
B-2100					
B-2101					

845

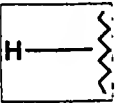
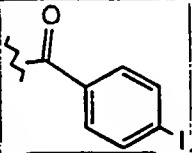
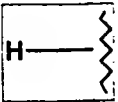
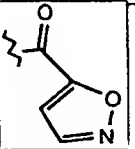
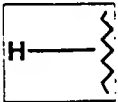
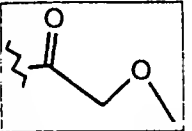
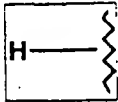
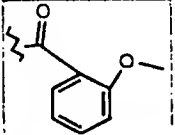
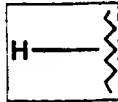
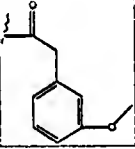
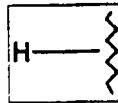
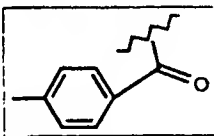
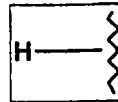
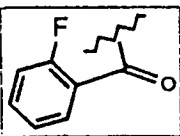
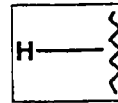
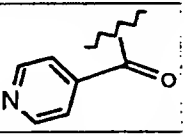
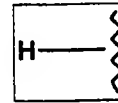
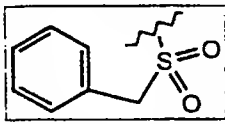
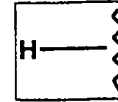
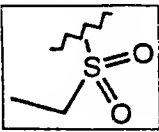


Examples B-2102 through B-2125 are prepared from Scaffold C-52

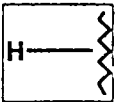
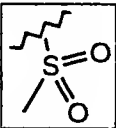
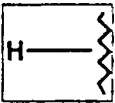
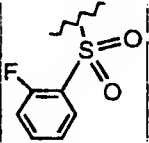
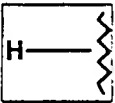
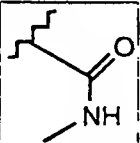
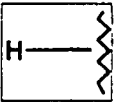
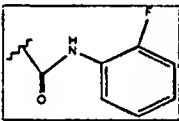
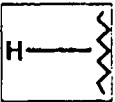
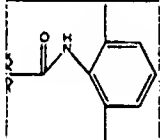
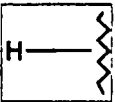
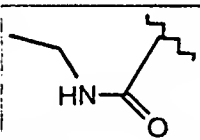
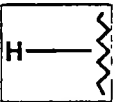
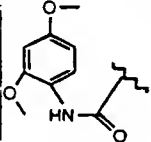
Example#	R <sup>2</sup>	R <sup>J</sup>			
B-2102					
B-2103					
B-2104					
B-2105					
B-2106					
B-2107					
B-2108					

Example#

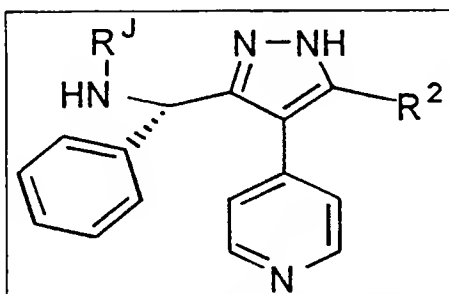
 $R^2$  $R^1$ 

B-2109					
B-2110					
B-2111					
B-2112					
B-2113					
B-2114					
B-2115					
B-2116					
B-2117					
B-2118					

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Example#	R <sup>2</sup>	R <sup>1</sup>			
B-2119					
B-2120					
B-2121					
B-2122					
B-2123					
B-2124					
B-2125					

848



Examples B-2126 through B-2149 are prepared from Scaffold C-56

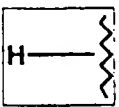
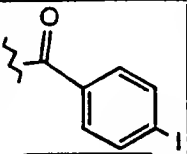
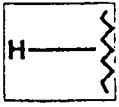
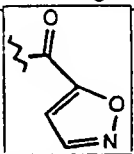
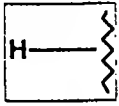
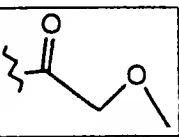
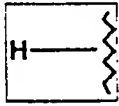
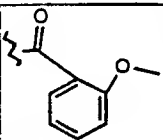
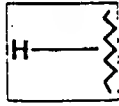
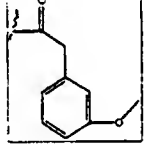
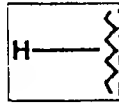
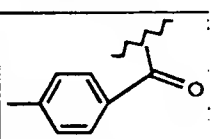
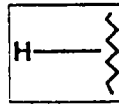
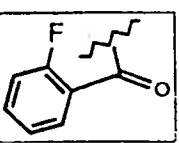
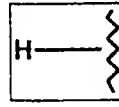
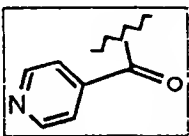
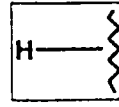
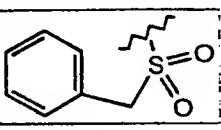
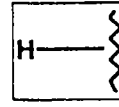
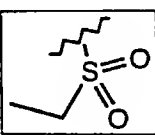
Example#

 $R^2$  $R^J$ 

B-2126					
B-2127					
B-2128					
B-2129					
B-2130					
B-2131					
B-2132					

Example#

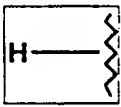
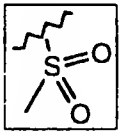
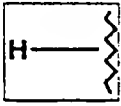
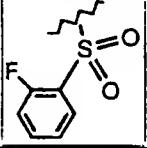
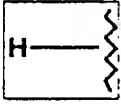
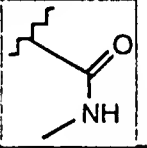
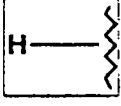
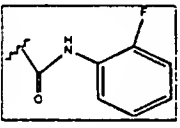
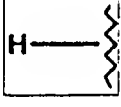
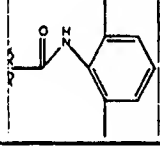
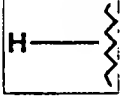
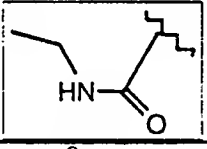
 $R^2$  $R^1$ 

B-2133					
B-2134					
B-2135					
B-2136					
B-2137					
B-2138					
B-2139					
B-2140					
B-2141					
B-2142					

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Example#

 $R^2$  $R^1$ 

B-2143					
B-2144					
B-2145					
B-2146					
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